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|      |    |        |   |
|------|----|--------|---|
| NEWS | 1  |        | Web Page URLs for STN Seminar Schedule - N. America   |
| NEWS | 2  | Apr 08 | "Ask CAS" for self-help around the clock  |
| NEWS | 3  | Jun 03 | New e-mail delivery for search results now available  |
| NEWS | 4  | Aug 08 | PHARMAMarketLetter(PHARMAML) - new on STN   |
| NEWS | 5  | Aug 19 | Aquatic Toxicity Information Retrieval (AQUIRE)<br>now available on STN                       |
| NEWS | 6  | Aug 26 | Sequence searching in REGISTRY enhanced   |
| NEWS | 7  | Sep 03 | JAPIO has been reloaded and enhanced  |
| NEWS | 8  | Sep 16 | Experimental properties added to the REGISTRY file  |
| NEWS | 9  | Sep 16 | CA Section Thesaurus available in CAPLUS and CA   |
| NEWS | 10 | Oct 01 | CASREACT Enriched with Reactions from 1907 to 1985  |
| NEWS | 11 | Oct 24 | BEILSTEIN adds new search fields  |
| NEWS | 12 | Oct 24 | Nutraceuticals International (NUTRACEUT) now available on STN                                 |
| NEWS | 13 | Nov 18 | DKILIT has been renamed APOLLIT   |
| NEWS | 14 | Nov 25 | More calculated properties added to REGISTRY  |
| NEWS | 15 | Dec 04 | CSA files on STN  |
| NEWS | 16 | Dec 17 | PCTFULL now covers WP/PCT Applications from 1978 to date                                      |
| NEWS | 17 | Dec 17 | TOXCENTER enhanced with additional content  |
| NEWS | 18 | Dec 17 | Adis Clinical Trials Insight now available on STN   |
| NEWS | 19 | Jan 29 | Simultaneous left and right truncation added to COMPENDEX,<br>ENERGY, INSPEC                  |
| NEWS | 20 | Feb 13 | CANCERLIT is no longer being updated  |
| NEWS | 21 | Feb 24 | METADEX enhancements  |
| NEWS | 22 | Feb 24 | PCTGEN now available on STN   |
| NEWS | 23 | Feb 24 | TEMA now available on STN   |
| NEWS | 24 | Feb 26 | NTIS now allows simultaneous left and right truncation  |
| NEWS | 25 | Feb 26 | PCTFULL now contains images   |
| NEWS | 26 | Mar 04 | SDI PACKAGE for monthly delivery of multifile SDI results                                     |
| NEWS | 27 | Mar 20 | EVENTLINE will be removed from STN  |
| NEWS | 28 | Mar 24 | PATDPAFULL now available on STN   |
| NEWS | 29 | Mar 24 | Additional information for trade-named substances without<br>structures available in REGISTRY |
| NEWS | 30 | Apr 11 | Display formats in DGENE enhanced   |
| NEWS | 31 | Apr 14 | MEDLINE Reload  |
| NEWS | 32 | Apr 17 | Polymer searching in REGISTRY enhanced  |
| NEWS | 33 | Apr 21 | Indexing from 1947 to 1956 being added to records in CA/CAPLUS                                |
| NEWS | 34 | Apr 21 | New current-awareness alert (SDI) frequency in<br>WPIDS/WPINDEX/WPIX                          |
| NEWS | 35 | Apr 28 | RDISCLOSURE now available on STN  |
| NEWS | 36 | May 05 | Pharmacokinetic information and systematic chemical names<br>added to PHAR                    |
| NEWS | 37 | May 15 | MEDLINE file segment of TOXCENTER reloaded  |
| NEWS | 38 | May 15 | Supporter information for ENCOMPPAT and ENCOMPLIT updated                                     |
| NEWS | 39 | May 16 | CHEMREACT will be removed from STN  |
| NEWS | 40 | May 19 | Simultaneous left and right truncation added to WSCA  |
| NEWS | 41 | May 19 | RAPRA enhanced with new search field, simultaneous left and                                   |

right truncation

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 13:02:29 ON 26 MAY 2003

|   |            |         |
|---|------------|---------|
| => FIL MEDLINE BIOSIS EMBASE CA SCISEARCH |            |         |
| COST IN U.S. DOLLARS                      | SINCE FILE | TOTAL   |
|   | ENTRY      | SESSION |
| FULL ESTIMATED COST                       | 0.21       | 0.21    |

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FILE 'SCISEARCH' ENTERED AT 13:02:49 ON 26 MAY 2003  
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=> s antisense or (comple (2n) (oligo? or nuclei?))  
L1 101549 ANTISENSE OR (COMPLE (2N) (OLIGO? OR NUCLEI?))

=> s antisense? or (comple? (2n) (oligo? or nuclei?))  
<-----User Break----->

SEARCH ENDED BY USER

=> s antisense? or (comple? (2n) (oligo? or nucle?))  
4 FILES SEARCHED...  
L2 217407 ANTISENSE? OR (COMPLE? (2N) (OLIGO? OR NUCLE?))

=> s ssdna or (singl? strand? (2n) (dna or rna or (nucle? acid?))  
UNMATCHED LEFT PARENTHESIS 'OR (SINGL?'  
The number of right parentheses in a query must be equal to the  
number of left parentheses.

=> s ssdna or (singl? strand? (2n) (dna or rna or (nucle? acid?)))  
3 FILES SEARCHED...  
L3 77824 SSDNA OR (SINGL? STRAND? (2N) (DNA OR RNA OR (NUCLE? ACID?)))

=> s l2 and l3  
L4 4019 L2 AND L3

=> s l2 (5n) l3  
L5 603 L2 (5N) L3

=> s l2 (3n) l3  
L6 474 L2 (3N) L3

=> s l6 and m13  
L7 26 L6 AND M13

=> dup rem l7  
PROCESSING COMPLETED FOR L7  
L8 15 DUP REM L7 (11 DUPLICATES REMOVED)

=> d l8 1-15 ibib abs

L8 ANSWER 1 OF 15 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 137:380940 CA  
TITLE: Unigene unidirectional antisense library derived from  
recombinant bacteriophage or phagemid vector for  
therapy and massive functional genomics  
INVENTOR(S): Park, Jong-Gu; Moon, Ik-Jae; Lee, Yun-Han  
PATENT ASSIGNEE(S): Welgene Pharmaceuticals, Inc., S. Korea  
SOURCE: PCT Int. Appl., 79 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 2002092807 | A1   | 20021121 | WO 2002-IB1753  | 20020516 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |

PRIORITY APPLN. INFO.: KR 2001-27071 A 20010517

AB The present invention provides a high throughput system for functional genomics using a unigene antisense library comprising large circular (LC)-antisense compds. The said large circular (LC)-antisense compds are derived from recombinant bacteriophage or phagemid vector. The antisense compds. were specific and effective for the elimination of target mRNA. Thus, the system of the present invention is used as temporary knock-down system to unveil functions of genes crit. for diseases. The system of the present invention can be adopted not only for functional genomics but also for effectively validating target for antisense or other mol. therapeutics against various malignancies, infections, and other diseases by blocking specific genes involved in the disease.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 15 CA COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 132:60106 CA  
 TITLE: Methods for generating highly diverse nucleic acid libraries  
 INVENTOR(S): Wagner, Richard; Wright, Martin C.; Kreider, Brent  
 PATENT ASSIGNEE(S): Phyllos, Inc., USA  
 SOURCE: PCT Int. Appl., 32 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2000000632   | A1   | 20000106 | WO 1999-US14776 | 19990629 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| AU 9948470  | A1   | 20000117 | AU 1999-48470   | 19990629 |
| EP 1092039  | A1   | 20010418 | EP 1999-932081  | 19990629 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |      |          |                 |          |
| JP 2002519038   | T2   | 20020702 | JP 2000-557385  | 19990629 |
| ZA 2000007261   | A    | 20020515 | ZA 2000-7261    | 20001207 |
| NO 2000006675   | A    | 20001228 | NO 2000-6675    | 20001228 |
| PRIORITY APPLN. INFO.: US 1998-90970P P 19980629  |      |          |                 |          |
| WO 1999-US14776 W 19990629  |      |          |                 |          |

AB Disclosed herein is a method for generating a nucleic acid library. The method first involves providing a population of single-stranded nucleic acid templates, each of the templates including a coding sequence and an operably linked promoter sequence. The population of single-stranded nucleic acid templates is hybridized to a mixt. of substantially **complementary single-stranded nucleic acid** fragments, the fragments being shorter in length than the nucleic acid template. Then each of the hybridization products of the 2nd step is contacted with both a DNA polymerase which lacks strand displacement activity and a DNA ligase under conditions in which the fragments act as primers for the completion of a second nucleic acid strand which is substantially complementary to the nucleic acid template. Finally, the products of the 3rd step are contacted with RNA polymerase to generate an RNA library, the library being transcribed from the second nucleic acid strand. In preferred embodiments, the method is used to introduce one or more mutations into the library. The invention also features a method for reducing sequence variation in a population of nucleic acid mols.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 15 MEDLINE DUPLICATE 1  
 ACCESSION NUMBER: 2000280072 MEDLINE  
 DOCUMENT NUMBER: 20280072 PubMed ID: 10773070  
 TITLE: Differential functional behavior of viral phi29, Nf and GA-1 SSB proteins.

AUTHOR: Gascon I; Lazaro J M; Salas M  
 CORPORATE SOURCE: Centro de Biologia Molecular 'Severo Ochoa' (CSIC-UAM),  
 Universidad Autonoma, Cantoblanco, 28049-Madrid, Spain.  
 CONTRACT NUMBER: 2R01 GM27242-20 (NIGMS)  
 SOURCE: NUCLEIC ACIDS RESEARCH, (2000 May 15) 28 (10) 2034-42.  
 Journal code: 0411011. ISSN: 1362-4962.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200006  
 ENTRY DATE: Entered STN: 20000706  
 Last Updated on STN: 20010521  
 Entered Medline: 20000626

AB DNA replication of phi29 and related phages takes place via a strand displacement mechanism, a process that generates large amounts of single-stranded DNA (ssDNA). Consequently, phage-encoded ssDNA-binding proteins (SSBs) are essential proteins during phage phi29-like DNA replication. In the present work we analyze the helix-destabilizing activity of the SSBs of phi29 and the related phages Nf and GA-1, their ability to eliminate non-productive binding of phi29 DNA polymerase to ssDNA and their stimulatory effect on replication by phi29 DNA polymerase in primed **M13** ssDNA replication, a situation that resembles type II replicative intermediates that occur during phi29-like DNA replication. Significant differences have been appreciated in the functional behavior of the three SSBs. First, the GA-1 SSB is able to display helix-destabilizing activity and to stimulate dNTP incorporation by phi29 DNA polymerase in the **M13** DNA replication assay, even at SSB concentrations at which the phi29 and Nf SSBs do not show any effect. On the other hand, the phi29 SSB is the only one of the three SSBs able to increase the replication rate of phi29 DNA polymerase in primed **M13** ssDNA replication. From the fact that the phi29 SSB, but not the Nf SSB, stimulates the replication rate of Nf DNA polymerase we conclude that the different behaviors of the SSBs on stimulation of the replication rate of phi29 and Nf DNA polymerases is most likely due to formation of different nucleoprotein complexes of the SSBs with the ssDNA rather than to a specific interaction between the SSB and the corresponding DNA polymerase. A model that correlates the thermodynamic parameters that define SSB-ssDNA nucleoprotein complex formation with the functional stimulatory effect of the SSB on phi29-like DNA replication has been proposed.

L8 ANSWER 4 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
 ACCESSION NUMBER: 2000:393645 SCISEARCH  
 THE GENUINE ARTICLE: 316CM  
 TITLE: Differential functional behavior of viral phi 29, Nf and GA-1 SSB proteins  
 AUTHOR: Gascon I; Lazaro J M; Salas M (Reprint)  
 CORPORATE SOURCE: UNIV AUTONOMA MADRID, CTR BIOL MOL SEVERO OCHOA, CSIC, UAM, E-28049 MADRID, SPAIN (Reprint); UNIV AUTONOMA MADRID, CTR BIOL MOL SEVERO OCHOA, CSIC, UAM, E-28049 MADRID, SPAIN  
 COUNTRY OF AUTHOR: SPAIN  
 SOURCE: NUCLEIC ACIDS RESEARCH, (15 MAY 2000) Vol. 28, No. 10, pp. 2034-2042.  
 Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.  
 ISSN: 0305-1048.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: English  
 REFERENCE COUNT: 54

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB DNA replication of phi 29 and related phages takes place via a strand displacement mechanism, a process that generates large amounts of single-stranded DNA (ssDNA). Consequently, phage-encoded ssDNA-binding proteins (SSBs) are essential proteins during phage phi 29-like DNA replication. In the present work we analyze the helix-destabilizing activity of the SSBs of phi 29 and the related phages Nf and GA-1, their ability to eliminate non-productive binding of phi 29 DNA polymerase to ssDNA and their stimulatory effect on replication by phi 29 DNA polymerase in primed **M13** ssDNA replication, a situation that resembles type II replicative intermediates that occur during phi 29-like DNA replication. Significant differences have been appreciated in the functional behavior of the three SSBs, First, the GA-1 SSB is able to display helix-destabilizing activity and to stimulate dNTP incorporation by phi 29 DNA polymerase in the **M13** DNA replication assay, even at SSB concentrations at which the phi 29 and Nf SSBs do not show any effect, On the other hand, the phi 29 SSB is the only one of the three SSBs able to increase the replication rate of phi 29 DNA polymerase in primed **M13** ssDNA replication. From the fact that the phi 29 SSB, but not the Nf SSB, stimulates the replication rate of Nf DNA polymerase we conclude that the different behaviors of the SSBs on stimulation of the replication rate of phi 29 and Nf DNA polymerases is most likely due to formation of different nucleoprotein complexes of the SSBs with the ssDNA rather than to a specific interaction between the SSB and the corresponding DNA polymerase. A model that correlates the thermodynamic parameters that define SSB-ssDNA **nucleoprotein complex** formation with the functional stimulatory effect of the SSB on phi 29-like DNA replication has been proposed.

L8 ANSWER 5 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 2000:190041 BIOSIS  
 DOCUMENT NUMBER: PREV200000190041  
 TITLE: Fluorescence and excitation Escherichia coli RecA protein spectra analyzed separately for tyrosine and tryptophan residues.  
 AUTHOR(S): Isaev-Ivanov, Vladimir V.; Kozlov, Mihail G.; Baitin, Dmitry M.; Masui, Ryoji; Kuramitsu, Seiki; Lanzov, Vladislav A. (1)  
 CORPORATE SOURCE: (1) Division of Molecular and Radiation Biophysics, Petersburg Nuclear Physics Institute, Russian Academy of Sciences, Gatchina, Saint Petersburg, 188350 Russia  
 SOURCE: Archives of Biochemistry and Biophysics, (April 1, 2000) Vol. 376, No. 1, pp. 124-140.  
 ISSN: 0003-9861.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB The method for separation of emission (EM) and excitation (EX) spectra of a protein into EM and EX spectra of its tyrosine (Tyr) and tryptophan (Trp) residues was described. The method was applied to analysis of Escherichia coli RecA protein and its complexes with Mg2+, ATPgammaS or ADP, and single-stranded DNA (ssDNA). RecA consists of a C-terminal domain containing two Trp and two Tyr residues, a major domain with five Tyr residues, and an N-terminal domain without these residues (R. M. Story, I. T. Weber, and T. A. Steitz (1992) Nature (London) 355, 374-376). Because the fluorescence of Tyr residues in the C-terminal domain was shown to be quenched by energy transfer to Trp residues, Trp and Tyr fluorescence of RecA was provided by the C-terminal and the major domains, respectively. Spectral analysis of Trp and Tyr constituents revealed that a relative spatial location of the C-terminal and the major domains in RecA monomers was different for their complexes with either ATPgammaS or ADP, whereas this location did not change upon additional interaction of these

complexes with ssDNA. Homogeneous (that is, independent of EX wavelength) and nonhomogeneous (dependent on EX wavelength) types of Tyr and Trp fluorescence quenching were analyzed for RecA and its **complexes** with **nucleotide** cofactors and **ssDNA**. The former was expected to result from singlet-singlet energy transfer from these residues to adenine of ATPgammaS or ADP. By analogy, the latter was suggested to proceed through energy transfer from high vibrational levels of the excited state of Trp and Tyr residues to the adenine. In this case, for correct calculation of the overlap integral, Trp and Tyr donor emission spectra were substituted by the spectral function of convolution of emission and excitation spectra that resulted in a significant increase of the overlap integral and gave an explanation of the nonhomogeneous quenching of Trp residues in the C-terminal domain.

L8 ANSWER 6 OF 15 MEDLINE DUPLICATE 2  
 ACCESSION NUMBER: 97141743 MEDLINE  
 DOCUMENT NUMBER: 97141743 PubMed ID: 8988001  
 TITLE: Gene V protein dimerization and cooperativity of binding of poly(dA).  
 AUTHOR: Terwilliger T C  
 CORPORATE SOURCE: Structural Biology Group, Los Alamos National Laboratory, New Mexico 87545, USA.  
 CONTRACT NUMBER: GM38714 (NIGMS)  
 SOURCE: BIOCHEMISTRY, (1996 Dec 24) 35 (51) 16652-64.  
 Journal code: 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199701  
 ENTRY DATE: Entered STN: 19970219  
 Last Updated on STN: 19970219  
 Entered Medline: 19970130

AB Gene V protein of bacteriophage  $\phi$ 1 is a dimeric protein that binds cooperatively to single-stranded nucleic acids. In order to determine whether a monomer-dimer equilibrium has an appreciable effect upon the thermodynamics of gene V protein binding to nucleic acids, the dissociation constant for the protein dimer was investigated using size-exclusion chromatography. At concentrations ranging from  $5 \times 10^{-10}$  to  $1.2 \times 10^{-5}$  M, the Stokes radius of the protein was that expected of the dimer of the gene V protein. The Stokes radius of the protein was also independent of salt concentration from 0.2 to 1.0 M NaCl in a buffer containing 10 mM Tris-HCl, pH 7.4, and 1 mM EDTA. The binding of the dimeric gene V protein to poly(dA) was studied using a simplified lattice model for protein-protein interactions adapted for use with a dimeric protein that binds simultaneously to two strands of nucleic acid. Interpretation of the salt dependence,  $C = [d \log(K_{int} \omega)]/[d \log(NaCl)]$ , of binding of such a dimeric protein to nucleic acid using the theory of Record et al. (Record, M. T., et al. (1976) J. Mol. Biol. 107, 145-158) indicates that C is a function of the numbers of cations and anions released from protein and nucleic acid upon binding of the dimer, not of the monomer. Cooperativity of gene V protein binding to poly(dA) was studied with titration experiments that are sensitive to the degree of cooperativity of binding. The cooperativity factor  $\omega$ , defined as the ratio of the binding constant for a site adjacent to a previously bound dimer to that for an isolated site, was found to be relatively insensitive to salt, with a value in the range of 2000-7000 for binding to poly(dA) at 3 degrees C and at 23 degrees C. This high cooperativity factor supports the suggestion that protein-protein contacts play a major role in the formation of the superhelical gene V protein-**single-stranded nucleic acid complex**.

L8 ANSWER 7 OF 15 CA COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 123:105487 CA  
 TITLE: Kinetic Studies by Fluorescence Resonance Energy  
 Transfer Employing a Double-Labeled Oligonucleotide:  
 Hybridization to the **Oligonucleotide  
 Complement and to Single-  
 Stranded DNA**  
 AUTHOR(S): Parkhurst, Kay M.; Parkhurst, Lawrence J.  
 CORPORATE SOURCE: Department of Chemistry, University of Nebraska  
 Lincoln, Lincoln, NE, 68588-0304, USA  
 SOURCE: Biochemistry (1995), 34(1), 285-92  
 CODEN: BICHAW; ISSN: 0006-2960  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A single 16-base oligodeoxyribonucleotide was labeled at the 3'-end with  
 fluorescein and at the 5'-end with x-rhodamine (R\*oligo\*F); the  
 chromophores served as a donor/acceptor pair, resp., for Forster resonance  
 energy transfer. We exploited the striking differences in the  
 steady-state emission spectra of the R\*oligo\*F as a single strand and in a  
 duplex structure to signal hybridization in soln. and to det. the kinetics  
 of duplex formation as the probe bound to its oligomer complement and to  
 its target sequence in M13mpl8(+) phage DNA. The binding followed  
 second-order kinetics; in 0.18 M NaCl (pH 8) with 25% formamide, the rate  
 const. for binding to the oligomer complement was 5.7 .times. 105 M-1 s-1,  
 and that to M13mpl8(+) was 5.7 .times. 104 M-1 s-1. The source of the  
 10-fold decrease in the rate of binding to M13mpl8(+) was examd. to  
 differentiate between multiple nonproductive nucleation and rapid  
 fluctuations in the structure around the target site. From simulations  
 based on each model combined with assocd. exptl. results, we concluded  
 that the slower binding was due to rapid structural fluctuations around  
 the target site, with an effective target concn. 0.1 of that of the total.  
 Comparisons of total fluorescein emission derived from both steady-state  
 and lifetime measurements suggest that the 5'-x-rhodamine induces a  
 conformational change that affects the interaction at the 3'-end between  
 the fluorescein and the polymer. The effects of salt on the fluorescence  
 were complex. The static quenching of fluorescein in the single-labeled,  
 single-stranded oligonucleotide did not change with NaCl (0-0.18 M),  
 whereas there were marked changes in the double-labeled probe, showing  
 that the conformational effects mediated by the 5'-x-rhodamine were salt  
 dependent.

L8 ANSWER 8 OF 15 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 95082803 MEDLINE  
 DOCUMENT NUMBER: 95082803 PubMed ID: 7990840  
 TITLE: [A new method of covalent immobilization of  
 oligodeoxyribonucleotides on nylon membranes for  
 hybridization with nucleic acids].  
 Novyi metod kovalentnoi immobilizatsii  
 oligodezoksiribonukleotidov na neilonovykh membranakh dlia  
 gibridizatsii s nukleinovymi kislotami.  
 AUTHOR: Ivanovskaia M G; Kozlov I A; Lebedeva I V; Shabarova Z A  
 SOURCE: MOLEKULIARNAIA BIOLOGIIA, (1994 Sep-Oct) 28 (5) 1176-82.  
 Journal code: 0105454. ISSN: 0026-8984.  
 PUB. COUNTRY: RUSSIA: Russian Federation  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: Russian  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199501  
 ENTRY DATE: Entered STN: 19950124  
 Last Updated on STN: 19950124  
 Entered Medline: 19950112



AB A new method of covalent immobilization of oligodeoxyribonucleotides on nylon membranes which contain surface amino groups was developed. The method consists in condensation between the amino group of the membrane and the carboxyl group of modified oligonucleotide by means of 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide. The carboxyl group was introduced into the oligonucleotide by means of postsynthetic attachment of peptide (reduced glutathione) at the terminal phosphate group of the oligonucleotide, using the N-hydroxybenzotriazole method of phosphate activation. Membranes containing a covalently immobilized 23-membered oligonucleotide were tested in hybridization with **complementary oligonucleotide**, and with **single-stranded DNA** of bacteriophage M13 which has a complementary sequence. The method of covalent immobilization is very simple and convenient. The membranes with covalently immobilized oligonucleotides may be used not only in hybridization analysis, but also for purification of nucleic acids and proteins which recognize nucleotide sequences and in sense biotechnology.

L8 ANSWER 9 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
 ACCESSION NUMBER: 95:191195 SCISEARCH  
 THE GENUINE ARTICLE: QL239  
 TITLE: NEW METHOD FOR COVALENT IMMOBILIZATION OF OLIGONUCLEOTIDES ON NYLON MEMBRANES  
 AUTHOR: IVANOVSKAYA M G (Reprint); KOZLOV I A; LEBEDEVA I V; SHABAROVA Z A  
 CORPORATE SOURCE: MOSCOW MV LOMONOSOV STATE UNIV, BELOZERSKII INST PHYSICOCHEM BIOL, MOSCOW 119899, RUSSIA (Reprint)  
 COUNTRY OF AUTHOR: RUSSIA  
 SOURCE: MOLECULAR BIOLOGY, (SEP/OCT 1994) Vol. 28, No. 5, Part 2, pp. 754-756.  
 ISSN: 0026-8933.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: ENGLISH  
 REFERENCE COUNT: 6

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB An efficient method was developed for covalent immobilization of oligodeoxyribonucleotides on commercially available nylon membranes containing amino groups. It is based on condensation of the membrane amino groups with the oligonucleotide carboxyls in the presence of 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide. Membranes containing an immobilized 23-membered oligonucleotide were hybridized with a **complementary oligonucleotide** and **single-stranded M13 DNA**. The membranes obtained could be used for hybridization analysis and isolation of nucleic acids and proteins recognizing certain sequences.

L8 ANSWER 10 OF 15 CA COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 113:94357 CA  
 TITLE: Methods for detecting nucleic acid sequences  
 INVENTOR(S): Duck, Peter; Bender, Robert  
 PATENT ASSIGNEE(S): Meigenics, Inc., USA  
 SOURCE: PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| WO 8910415 | A1   | 19891102 | WO 1989-US1825  | 19890428 |

W: AU, DK, JP  
 RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE  
 US 5011769 A 19910430 US 1988-187814 19880429  
 AU 8935697 A1 19891124 AU 1989-35697 19890428  
 EP 365663 A1 19900502 EP 1989-905902 19890428  
 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE  
 JP 02504110 T2 19901129 JP 1989-505932 19890428  
 JP 2839608 B2 19981216  
 DK 8906658 A 19900202 DK 1989-6658 19891222  
 PRIORITY APPLN. INFO.: US 1988-187814 19880429  
 US 1985-805279 19851205  
 WO 1989-US1825 19890428

AB Target nucleic acid sequences are detected by (a) forming a reaction mixt. which includes the target and an amt. of a **complementary single-stranded nucleic acid probe** which is greater than the target under conditions which allow the probe and target to hybridize; (b) nicking the hybridized probe at least once within a predetd. sequence to form .gtoreq.2 probe fragments hybridized to the target, resulting in the probe fragments becoming single-stranded and allowing the target nucleic acid to hybridize to another probe; (c) identifying the probe fragments, thereby detecting the target nucleic acid. The probe comprises [NA1RNA2]n (NA1, NA2 = nucleic acid sequences; R = RNA sequence; n = 1-10) and is nicked with a double-stranded RNase. Probes [e.g. 5'-d(CCAGGTT)r(UUCCC)d(AGTCACG)3'] were labeled with [32P]-ATP and incubated with target DNA at 65.degree. for 10 min and at 37.degree. for 30 min. RNase H was then added at 0, 10, and 20 min. After 30 min the mixt. was loaded with formamide dye on a 0.8 mm 20% acrylamide/7 M urea gel at 800 V with a heating plate. The sensitivity was ~10-19-10-20 mol target.

L8 ANSWER 11 OF 15 MEDLINE DUPLICATE 4  
 ACCESSION NUMBER: 88224566 MEDLINE  
 DOCUMENT NUMBER: 88224566 PubMed ID: 3286164  
 TITLE: Site-specific oligonucleotide-directed mutagenesis using T4 DNA polymerase.  
 AUTHOR: Chang G J; Johnson B J; Trent D W  
 CORPORATE SOURCE: Division of Vector-Borne Viral Diseases, Centers for Disease Control, Fort Collins, CO 80522.  
 SOURCE: DNA, (1988 Apr) 7 (3) 211-7.  
 Journal code: 8302432. ISSN: 0198-0238.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198806  
 ENTRY DATE: Entered STN: 19900308  
 Last Updated on STN: 19980206  
 Entered Medline: 19880627

AB A simple and efficient mutagenesis procedure is described which uses both the 3'----5' exonuclease and 5'----3' polymerase activities of T4 DNA polymerase. Different types of mutation-deletion, insertion, and substitution-can be introduced into the DNA in a single reaction. The technique uses recombinant **M13 single-stranded DNA** and two **complementary DNA oligonucleotides** to target and control the extent of deletions catalyzed by T4 DNA polymerase. The second oligonucleotide not only directs ligation, but also serves as a template for insertion or substitution of nucleotides by T4 polymerase. Mutant phages in a genetically pure form can be obtained at high efficiency, allowing their characterization directly by nucleotide sequencing without prior enrichment, plaque purification, and screening. We tested the versatility of this method by manipulating five regions of cDNA encoding the structural proteins of eastern equine encephalitis

virus.

L8 ANSWER 12 OF 15 MEDLINE DUPLICATE 5  
ACCESSION NUMBER: 88062759 MEDLINE  
DOCUMENT NUMBER: 88062759 PubMed ID: 3316669  
TITLE: Solution hybridization of crosslinkable DNA  
oligonucleotides to bacteriophage **M13** DNA. Effect  
of secondary structure on hybridization kinetics and  
equilibria.  
AUTHOR: Gamper H B; Cimino G D; Hearst J E  
CORPORATE SOURCE: HRI Research Incorporated, Berkeley, CA 94710.  
CONTRACT NUMBER: GM 11180 (NIGMS)  
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1987 Sep 20) 197 (2) 349-62.  
Journal code: 2985088R. ISSN: 0022-2836.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198801  
ENTRY DATE: Entered STN: 19900305  
Last Updated on STN: 19970203  
Entered Medline: 19880112

AB Several DNA oligonucleotides have been photochemically modified with the  
furocoumarin 4'-hydroxymethyl-4,5',8-trimethylpsoralen (HMT) such that  
each contained a single HMT furan side monoadduct to thymidine at a unique  
5' T<sub>p</sub>A 3' sequence. When these oligonucleotides were hybridized to their  
respective complements, the HMT adduct could be driven to form an  
interstrand crosslink by irradiation of the hybrid with 360 nm light. The  
ability to crosslink probe-target complexes has allowed us to determine  
the kinetics and the extent of hybridization in solution between these  
**oligonucleotides** and their **complementary** sequences in  
**single-stranded bacteriophage M13 DNA**  
. Our data indicate that these parameters are strongly influenced by the  
existence of local as well as global secondary structure in the viral DNA.  
During hybridization, rearrangement of this secondary structure so as to  
expose the target sequence can be rate-limiting. Upon attainment of  
equilibrium, only a portion of the target sequence may be hybridized to  
the probe with the remainder involved in intrastrand base-pairing. Using  
crosslinkable oligonucleotide probes hybridized and irradiated near the  
melting temperature of the respective probe-target complex one can  
partially overcome these secondary structure effects.

L8 ANSWER 13 OF 15 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 107:3125 CA  
TITLE: Restriction of single-stranded **M13** DNA using  
synthetic oligonucleotides: the structural  
requirement of restriction enzymes  
AUTHOR(S): Qi, Guorong; Wong, Pierre; Cedergren, Robert  
CORPORATE SOURCE: Dep. Biochem., Univ. Montreal, Montreal, QC, H3C 3J7,  
Can.  
SOURCE: Biochemistry and Cell Biology (1987), 65(1), 50-5  
CODEN: BCBIEQ; ISSN: 0829-8211  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A targeted ss (single-stranded) DNA cleavage technique is reported which  
involves the use of a synthetic oligomers complementary to the ss  
**M13** DNA polylinker. BamH1, SmaI, And KpnI restriction enzymes  
were tested with a partial duplex DNA formed from ss **M13** DNA and  
a nested series of fragments derived from a synthetic 21-mer which were  
complementary to the polylinker region. These enzymes require .ltoreq.2  
flanking nucleotides in addn. to the hexameric recognition site for  
efficient cleavage. Thus, this technique could be useful for effecting

unique cleavages of DNA with enzymes which generally give a large no. of fragments and for strategies of ss DNA manipulation.

L8 ANSWER 14 OF 15 MEDLINE DUPLICATE 6  
ACCESSION NUMBER: 85191078 MEDLINE  
DOCUMENT NUMBER: 85191078 PubMed ID: 3991809  
TITLE: A rapid single-stranded cloning strategy for producing a sequential series of overlapping clones for use in DNA sequencing: application to sequencing the corn mitochondrial 18 S rDNA.  
AUTHOR: Dale R M; McClure B A; Houchins J P  
CONTRACT NUMBER: 5T32 GM07094 (NIGMS)  
GM321113 (NIGMS)  
SOURCE: PLASMID, (1985 Jan) 13 (1) 31-40.  
Journal code: 7802221. ISSN: 0147-619X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-M10248  
ENTRY MONTH: 198506  
ENTRY DATE: Entered STN: 19900320  
Last Updated on STN: 19970203  
Entered Medline: 19850612  
AB A simple new procedure was described for producing a sequential series of overlapping clones for use in DNA sequencing. The technique used **single-stranded M13 DNA** and **complementary DNA oligomers** to form specific cleavage and ligation substrates. It was, therefore, independent of the sequence of the DNA cloned into the vector. Deletions of varying sizes were generated from one end of the insert through the 3' to 5' exonuclease activity of T4 DNA polymerase. The approximate size of the deletion and therefore the starting point for DNA sequencing could be estimated by electrophoresis of the subcloned phage DNA on a agarose gel. This greatly reduced the number of templates that must be sequenced to obtain a complete sequence. The entire procedure could be carried out in one tube in less than a day. The procedure was used to subclone and sequence the maize mitochondrial 18 S rDNA and 5' flanking region (2622 bases) in less than a week. Other applications of oligomers and single-stranded DNA in the construction of insertions, deletions, and cDNAs are discussed.

L8 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7  
ACCESSION NUMBER: 1985:351769 BIOSIS  
DOCUMENT NUMBER: BA80:21761  
TITLE: THE ORIGIN OF THE HELPER COMPONENT OF TOBACCO VEIN MOTTLING VIRUS TRANSLATIONAL INITIATION NEAR THE 5' TERMINUS OF THE VIRAL RNA AND TERMINATION BY UAG CODONS.  
AUTHOR(S): HELLMANN G M; SHAW J G; RHOADS R E  
CORPORATE SOURCE: DEP. BIOCHEM., UNIV. KY., LEXINGTON, KY. 40536.  
SOURCE: VIROLOGY, (1985) 143 (1), 23-34.  
CODEN: VIRLAX. ISSN: 0042-6822.  
FILE SEGMENT: BA; OLD  
LANGUAGE: English  
AB The nature of the polypeptide products encoded by the 5'-terminal region of the RNA of the potyvirus, tobacco vein mottling virus (TVMV), was investigated. **Single-stranded DNA** probes **complementary** to either **nucleotides** 1100-2100 or 2100-2820 from the 5' terminus of the RNA were prepared by subcloning recombinant plasmids in bacteriophage **M13**. These were hybridized to TVMV RNA, the DNA:RNA hybrids translated in a reticulocyte lysate cell-free translation system (hybrid-arrested translation), and the

products analyzed by electrophoresis on sodium dodecyl sulfate-containing polyacrylamide gels. The hybrids produced altered patterns of polypeptides which indicated that the major products, P75, was translated from the 5' terminus of the RNA. The N-terminal portion (MW .apprx. 35,000) of P75 did not react with antisera to any of the 5 known potyviral protein, suggesting the existence of a previously unidentified cistron at the 5' terminus. Translation of additional RNA sequences produced a polypeptide with a MW of 68,000 which was immunoprecipitable by antiserum to TVMV helper component, establishing the coding region for helper component near the 5' terminus. Limited DNA sequence analysis of the region encoding the C terminus of P75 revealed an open reading frame of 369 nucleotides followed by a pair of UAG codons. Pulse-chase experiments demonstrated that in the first 10 min of incubation, the only polypeptidase initiated was P75, suggesting that products downstream from P75 arose from in vitro fragmentation of TVMV RNA and translation of the RNA fragments.

=> d his

(FILE 'HOME' ENTERED AT 13:02:29 ON 26 MAY 2003)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:02:49 ON 26 MAY 2003

```
L1      101549 S ANTISENSE OR (COMPLE (2N) (OLIGO? OR NUCLEI?))
L2      217407 S ANTISENSE? OR (COMPLE? (2N) (OLIGO? OR NUCLE?))
L3      77824 S SSDNA OR (SINGL? STRAND? (2N) (DNA OR RNA OR (NUCLE? ACID?)))
L4      4019 S L2 AND L3
L5      603 S L2 (5N) L3
L6      474 S L2 (3N) L3
L7      26 S L6 AND M13
L8      15 DUP REM L7 (11 DUPLICATES REMOVED)
```

=> s antisense or (comple (2n) (oligo? or nucle?))

<-----User Break----->

SEARCH ENDED BY USER

SEARCH ENDED BY USER

=> s antisense or (complem? (2n) (oligo? or nucle?))

<-----User Break----->

SEARCH ENDED BY USER

SEARCH ENDED BY USER

=> s antisense? or (complem? (2n) (oligo? or nucle?))

```
L9      123487 ANTISENSE? OR (COMPLEM? (2N) (OLIGO? OR NUCLE?))
```

=> s antisense? or (anti (n) sense) or (complem? (2n) (oligo? or nucle?))

```
L10     126636 ANTISENSE? OR (ANTI (N) SENSE) OR (COMPLEM? (2N) (OLIGO? OR
      NUCLE?))
```

=> s l10 and m13

```
L11     231 L10 AND M13
```

=> s l10 (2n) m 13

```
L12     1 L10 (2N) M 13
```

=> s l10 (2n) m13

```
L13     9 L10 (2N) M13
```

=> dup rem l13

PROCESSING COMPLETED FOR L13

L14

6 DUP REM L13 (3 DUPLICATES REMOVED)

=&gt; d l14 1-6 ibib abs

L14 ANSWER 1 OF 6 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER:

137:364368 CA

TITLE:

Libraries of RNAs that can be prepared as large circular molecules and their use in high throughput screening and functional genomics

INVENTOR(S):

Park, Jong-Gu; Moon, Ik-Jae; Lee, Yun-Han

PATENT ASSIGNEE(S):

Welgene, Inc., S. Korea

SOURCE:

PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 2002092808 | A1   | 20021121 | WO 2002-IB735   | 20020309 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |

PRIORITY APPLN. INFO.:

KR 2001-27071 A 20010517

AB The present invention provides a high-throughput system for functional genomics using a random gene unidirectional antisense library comprising large circular RNAs including on or more an antisense segments. The antisense RNAs are specific and effective inhibitors of translation of a target mRNA. Thus, the system may be effectively used as temporary knock-down system to unveil functions of genes crit. for diseases. The RNA sequences are obtained from a specific biol. state, such as a disease state, by methods such as subtractive hybridization. The selected sequences may then be used to selectively inhibit state-specific genes. These large sequences are generated from bacteriophage or phagemid clones and because they may be several hundred or thousand base pairs long, they are accurate and specific in their effects. Use of bacteriophage M13 and phagemids to generate large circular RNAs inhibiting expression of genes for tumor necrosis factor .alpha. and NF-.kappa.B is demonstrated. The system of the present invention can be adapted not only for functional genomics but also for effectively validating target for antisense or other mol. therapeutics against various malignancies, infections, and other diseases by blocking specific genes involved in the disease.

REFERENCE COUNT:

9

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 6 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER:

134:142799 CA

TITLE:

Plasmodium falciparum carbamoyl phosphate synthetase II gene sequence and production of ribozymes, antisense molecules and other gene inactivation agents designed from this sequence

INVENTOR(S):

Stewart, Thomas S.; Flores, Maria V.; O'sullivan, William J.

PATENT ASSIGNEE(S):

Unisearch Ltd., Australia

SOURCE: U.S., 32 pp., Cont.-in-part of U.S. 5,849,573.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| US 6183996  | B1   | 20010206 | US 1998-150741  | 19980910    |
| WO 9412643  | A1   | 19940609 | WO 1993-AU617   | 19931202    |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN |      |          |                 |             |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG                                    |      |          |                 |             |
| ZA 9309080  | A    | 19940805 | ZA 1993-9080    | 19931203    |
| US 5849573  | A    | 19981215 | US 1995-446855  | 19950706    |
| PRIORITY APPLN. INFO.:  |      |          | AU 1992-6206    | A 19921203  |
|   |      |          | AU 1992-6380    | A 19921216  |
|   |      |          | WO 1993-AU617   | W 19931202  |
|   |      |          | US 1995-446855  | A2 19950706 |

AB The present invention provides a nucleotide sequence encoding carbamoyl phosphate synthetase II of Plasmodium falciparum. Carbamoyl phosphate synthetase II catalyzes the first committed and rate-limiting step in the de novo pyrimidine biosynthetic pathway. P. falciparum relies exclusively on pyrimidine synthesis de novo because of its inability to salvage pyrimidines. Mature human red blood cells, however, have no recognized requirement for a pyrimidine nucleotide. Accordingly, this enzyme represents a prime chemotherapeutic locus. The present invention relates to the use of the sequence encoding carbamoyl phosphate synthetase II in the recombinant prodn. of carbamoyl phosphate synthetase II and to antisense mols., ribozymes and other gene inactivation agents designed from this sequence.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 6 CA COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 119:242934 CA  
 TITLE: Photocleavage of DNA using organic oxyradicals  
 INVENTOR(S): Herkstroeter, William George; Farid, Samir Yacoub; Gould, Ian Robert; Chen, Chin Hsin; Jayaraman, Krishna; Specht, Donald P.  
 PATENT ASSIGNEE(S): Eastman Kodak Co., USA  
 SOURCE: PCT Int. Appl., 56 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO.9314104   | A1   | 19930722 | WO 1993-US256   | 19930113 |
| W: CA, JP  |      |          |                 |          |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |          |
| PRIORITY APPLN. INFO.:   |      |          | US 1992-819905  | 19920113 |
|  |      |          | US 1993-1362    | 19930107 |

OTHER SOURCE(S): MARPAT 119:242934

AB Compns. for photocleavage of DNA comprise an oligonucleotide conjugated to an org. oxyradical precursor. The precursor can produce an oxyradical by direct photoexcitation, or by accepting an electron from a dye followed by

release of an oxyradical. Upon exposure of a soln. contg. the target DNA and the conjugate (and a dye if necessary) to activating light, an oxyradical is produced and the sugar-phosphate backbone of the target is cleaved. Alternatively, the oligonucleotide can be conjugated to the dye. A conjugate of acridine orange and **M13-complementary oligonucleotide** was prepd. Exposure of a soln. of M13, dye-oligonucleotide conjugate, and oxyradical precursor 1,5-bis-(stilbazole-N-oxide)-pentane to light of appropriate wavelength resulted in cleavage of M13 in only one confined region of the entire DNA sequence.

L14 ANSWER 4 OF 6 CA COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 114:1791 CA  
 TITLE: Detection of nucleic acid sequences using particle agglutination  
 INVENTOR(S): Olson, Jeffrey C.  
 PATENT ASSIGNEE(S): Angenics, Inc., USA  
 SOURCE: PCT Int. Appl., 64 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| WO 9002205 | A1   | 19900308 | WO 1989-US3624  | 19890823 |

W: JP

RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

PRIORITY APPLN. INFO.: US 1988-236535 19880825

AB A target nucleic acid in a sample is detected using .gtoreq.2 noncomplementary nucleic acid probes which can hybridize to two nonoverlapping areas of the target sequence, these probes are labeled with .gtoreq.1 mol. of one member of a specific binding pair, and with particles carrying the 2nd member of the specific binding pair and allowing the probes to hybridize with the target nucleic acid. The target nucleic acid hybridized to the two oligonucleotide probes are then bound by the particles with the formation of crosslinked aggregates. This agglutination can be detected. Two different 15-residue **oligonucleotides** which were **complementary to M13** mp18 DNA and which were biotinylated were added to M13mp18. Biotinylated DNA was produced by the polymerase chain reaction. This amplified DNA was added to streptavidin-or avidin-latex conjugates. The presence of the M13mp18 target DNA was indicated by agglutination of the latex particles.

L14 ANSWER 5 OF 6 MEDLINE DUPLICATE 1  
 ACCESSION NUMBER: 90076481 MEDLINE  
 DOCUMENT NUMBER: 90076481 PubMed ID: 2480250  
 TITLE: The algorithm of estimation of the Km values for primers of various structure and length in the polymerization reaction catalyzed by Klenow fragment of DNA polymerase I from E. coli.  
 AUTHOR: Nevinsky G A; Nemudraya A V; Levina A S; Khomov V V  
 CORPORATE SOURCE: Novosibirsk Institute of Bioorganic Chemistry, Siberian Division of the USSR Academy of Sciences, Novosibirsk.  
 SOURCE: FEBS LETTERS, (1989 Nov 20) 258 (1) 166-70.  
 Journal code: 0155157. ISSN: 0014-5793.  
 PUB. COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199001



ENTRY DATE: Entered STN: 19900328  
Last Updated on STN: 19980206  
Entered Medline: 19900123

AB DNA synthesis at primers d(pT)n, d(pA)n, d(pC)n, and d(pG)n in the presence of corresponding complementary templates and at hetero-**oligoprimers complementary** to M13 phage DNA was investigated. The values of both -log Km and log Vmax increased linearly if homo-oligoprimers contained less than 10 nucleotides. The lengthening of d(pT)n and d(pA)n primers by one mononucleotide unit (n = 1-10) resulted in the 1.82-fold decrease of the Km values. The incremental decreases of Km for d(pC)n and d(pG)n were equal to about 2.46. The enhancement of the homo- and hetero-oligonucleotide primers' affinity to the enzyme due to one Watson-Crick hydrogen bond between complementary template and primer is about 1.35 times. This allows to calculate the Km values for primers of various structure and length up to 10 units. The objective laws of the Km and Vmax values changes for primers containing more than 10 nucleotides were analyzed.

L14 ANSWER 6 OF 6 MEDLINE DUPLICATE 2  
ACCESSION NUMBER: 85191078 MEDLINE  
DOCUMENT NUMBER: 85191078 PubMed ID: 3991809  
TITLE: A rapid single-stranded cloning strategy for producing a sequential series of overlapping clones for use in DNA sequencing: application to sequencing the corn mitochondrial 18 S rDNA.  
AUTHOR: Dale R M; McClure B A; Houchins J P  
CONTRACT NUMBER: 5T32 GM07094 (NIGMS)  
GM32113 (NIGMS)  
SOURCE: PLASMID, (1985 Jan) 13 (1) 31-40.  
Journal code: 7802221. ISSN: 0147-619X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-M10248  
ENTRY MONTH: 198506  
ENTRY DATE: Entered STN: 19900320  
Last Updated on STN: 19970203  
Entered Medline: 19850612

AB A simple new procedure was described for producing a sequential series of overlapping clones for use in DNA sequencing. The technique used single-stranded M13 DNA and **complementary** DNA **oligomers** to form specific cleavage and ligation substrates. It was, therefore, independent of the sequence of the DNA cloned into the vector. Deletions of varying sizes were generated from one end of the insert through the 3' to 5' exonuclease activity of T4 DNA polymerase. The approximate size of the deletion and therefore the starting point for DNA sequencing could be estimated by electrophoresis of the subcloned phage DNA on a agarose gel. This greatly reduced the number of templates that must be sequenced to obtain a complete sequence. The entire procedure could be carried out in one tube in less than a day. The procedure was used to subclone and sequence the maize mitochondrial 18 S rDNA and 5' flanking region (2622 bases) in less than a week. Other applications of oligomers and single-stranded DNA in the construction of insertions, deletions, and cDNAs are discussed.

=> d his

(FILE 'HOME' ENTERED AT 13:02:29 ON 26 MAY 2003)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:02:49 ON 26

MAY 2003

L1 101549 S ANTISENSE OR (COMPLE (2N) (OLIGO? OR NUCLEI?))  
L2 217407 S ANTISENSE? OR (COMPLE? (2N) (OLIGO? OR NUCLE?))  
L3 77824 S SSDNA OR (SINGL? STRAND? (2N) (DNA OR RNA OR (NUCLE? ACID?)))  
L4 4019 S L2 AND L3  
L5 603 S L2 (5N) L3  
L6 474 S L2 (3N) L3  
L7 26 S L6 AND M13  
L8 15 DUP REM L7 (11 DUPLICATES REMOVED)  
L9 123487 S ANTISENSE? OR (COMPLEM? (2N) (OLIGO? OR NUCLE?))  
L10 126636 S ANTISENSE? OR (ANTI (N) SENSE) OR (COMPLEM? (2N) (OLIGO? OR N  
L11 231 S L10 AND M13  
L12 1 S L10 (2N) M 13  
L13 9 S L10 (2N) M13  
L14 6 DUP REM L13 (3 DUPLICATES REMOVED)

=> s l3 and m13

L15 2854 L3 AND M13

=> s l15 and l10

L16 69 L15 AND L10

=> s l16 and (circ? (5n) l10)

L17 1 L16 AND (CIRC? (5N) L10)

=> d l17 ibib abs

L17 ANSWER 1 OF 1 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 137:380940 CA

TITLE: Unigene unidirectional **antisense** library  
derived from recombinant bacteriophage or phagemid  
vector for therapy and massive functional genomics  
INVENTOR(S): Park, Jong-Gu; Moon, Ik-Jae; Lee, Yun-Han  
PATENT ASSIGNEE(S): Welgene Pharmaceuticals, Inc., S. Korea  
SOURCE: PCT Int. Appl., 79 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2002092807   | A1   | 20021121 | WO 2002-IB1753  | 20020516 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,<br>GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,<br>LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,<br>PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,<br>UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,<br>TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,<br>CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,<br>BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |

PRIORITY APPLN. INFO.: KR 2001-27071 A 20010517

AB The present invention provides a high throughput system for functional genomics using a unigene **antisense** library comprising large **circular** (LC)-**antisense** compds. The said large **circular** (LC)-**antisense** compds are derived from recombinant bacteriophage or phagemid vector. The **antisense** compds. were specific and effective for the elimination of target mRNA. Thus, the system of the present invention is used as temporary knock-down

system to unveil functions of genes crit. for diseases. The system of the present invention can be adopted not only for functional genomics but also for effectively validating target for **antisense** or other mol. therapeutics against various malignancies, infections, and other diseases by blocking specific genes involved in the disease.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 13:02:29 ON 26 MAY 2003)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:02:49 ON 26 MAY 2003

L1 101549 S ANTISENSE OR (COMPLE (2N) (OLIGO? OR NUCLEI?))  
L2 217407 S ANTISENSE? OR (COMPLE? (2N) (OLIGO? OR NUCLE?))  
L3 77824 S SSDNA OR (SINGL? STRAND? (2N) (DNA OR RNA OR (NUCLE? ACID?)))  
L4 4019 S L2 AND L3  
L5 603 S L2 (5N) L3  
L6 474 S L2 (3N) L3  
L7 26 S L6 AND M13  
L8 15 DUP REM L7 (11 DUPLICATES REMOVED)  
L9 123487 S ANTISENSE? OR (COMPLEM? (2N) (OLIGO? OR NUCLE?))  
L10 126636 S ANTISENSE? OR (ANTI (N) SENSE) OR (COMPLEM? (2N) (OLIGO? OR N  
L11 231 S L10 AND M13  
L12 1 S L10 (2N) M 13  
L13 9 S L10 (2N) M13  
L14 6 DUP REM L13 (3 DUPLICATES REMOVED)  
L15 2854 S L3 AND M13  
L16 69 S L15 AND L10  
L17 1 S L16 AND (CIRC? (5N) L10)

=> s (circ? (5n) l10)  
L18 186 (CIRC? (5N) L10)

=> s l18 and m13  
L19 3 L18 AND M13

=> dup rem l19  
PROCESSING COMPLETED FOR L19  
L20 3 DUP REM L19 (0 DUPLICATES REMOVED)

=> d l20 1-3 ibib abs

L20 ANSWER 1 OF 3 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 137:364368 CA  
TITLE: Libraries of RNAs that can be prepared as large  
circular molecules and their use in high throughput  
screening and functional genomics  
INVENTOR(S): Park, Jong-Gu; Moon, Ik-Jae; Lee, Yun-Han  
PATENT ASSIGNEE(S): Welgene, Inc., S. Korea  
SOURCE: PCT Int. Appl., 87 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2002092808 | A1   | 20021121 | WO 2002-IB735   | 20020309 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: KR 2001-27071 A 20010517

AB The present invention provides a high-throughput system for functional genomics using a random gene unidirectional **antisense** library comprising large **circular** RNAs including on or more an antisense segments. The antisense RNAs are specific and effective inhibitors of translation of a target mRNA. Thus, the system may be effectively used as temporary knock-down system to unveil functions of genes crit. for diseases. The RNA sequences are obtained from a specific biol. state, such as a disease state, by methods such as subtractive hybridization. The selected sequences may then be used to selectively inhibit state-specific genes. These large sequences are generated from bacteriophage or phagemid clones and because they may be several hundred or thousand base pairs long, they are accurate and specific in their effects. Use of bacteriophage **M13** and phagemids to generate large circular RNAs inhibiting expression of genes for tumor necrosis factor .alpha. and NF-.kappa.B is demonstrated. The system of the present invention can be adapted not only for functional genomics but also for effectively validating target for antisense or other mol. therapeutics against various malignancies, infections, and other diseases by blocking specific genes involved in the disease.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 3 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 137:380940 CA

TITLE: Unigene unidirectional antisense library derived from recombinant bacteriophage or phagemid vector for therapy and massive functional genomics

INVENTOR(S): Park, Jong-Gu; Moon, Ik-Jae; Lee, Yun-Han

PATENT ASSIGNEE(S): Welgene Pharmaceuticals, Inc., S. Korea

SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 2002092807 | A1   | 20021121 | WO 2002-IB1753  | 20020516 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |

PRIORITY APPLN. INFO.: KR 2001-27071 A 20010517

AB The present invention provides a high throughput system for functional

genomics using a unigene **antisense** library comprising large **circular** (LC)-**antisense** compds. The said large **circular** (LC)-**antisense** compds are derived from recombinant bacteriophage or phagemid vector. The antisense compds. were specific and effective for the elimination of target mRNA. Thus, the system of the present invention is used as temporary knock-down system to unveil functions of genes crit. for diseases. The system of the present invention can be adopted not only for functional genomics but also for effectively validating target for antisense or other mol. therapeutics against various malignancies, infections, and other diseases by blocking specific genes involved in the disease.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 3 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 137:227643 CA

TITLE: Large **circular** target-specific **antisense** nucleic acids for inhibition of gene expression and therapy

INVENTOR(S): Park, Jong-gu; Huh, Bin

PATENT ASSIGNEE(S): Welgene Inc., S. Korea

SOURCE: Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 1239034  | A2   | 20020911 | EP 2002-4933    | 20020305 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR |      |          |                 |          |
| US 2002182181   | A1   | 20021205 | US 2002-66498   | 20020130 |
| AU 2002018831   | A5   | 20020912 | AU 2002-18831   | 20020228 |
| CN 1374316  | A    | 20021016 | CN 2002-107110  | 20020308 |
| US 2002168631   | A1   | 20021114 | US 2002-94183   | 20020308 |

PRIORITY APPLN. INFO.: KR 2001-12061 A 20010308  
WO 2001-KR1730 A 20011013

AB The present application describes a large **circular** target-specific **antisense** mol. that is effective in ablating RNA and protein expression. The large **circular antisense** mol. is used to treat any human disease in which modulation of gene expression can be beneficial to intervene in the disease initiation and progression. Thus, large circular nucleic acid mols. were constructed employing a phagemid vector and the M13KO7 helper bacteriophages contg. the antisense sequence for TNF-.alpha., NF-.kappa.B, c-myc, c-myb, c-Ki-ras, and cdk2. TNF.alpha.-M13AS was tested for its circular structure and stability to nucleases. The antisense mols. specifically reduced expression of their resp. mRNA, and inhibited growth of cancer cells.

=> s park, J?/au; s Moon, I?/au

L21 35781 PARK, J?/AU

L22 800 MOON, I?/AU

=> s (l21 or l22) and m13

L23 8 (L21 OR L22) AND M13

=> dup rem 123  
PROCESSING COMPLETED FOR L23  
L24 5 DUP REM L23 (3 DUPLICATES REMOVED)

=> d his

(FILE 'HOME' ENTERED AT 13:02:29 ON 26 MAY 2003)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:02:49 ON 26  
MAY 2003

L1 101549 S ANTISENSE OR (COMPLE (2N) (OLIGO? OR NUCLEI?))  
L2 217407 S ANTISENSE? OR (COMPLE? (2N) (OLIGO? OR NUCLE?))  
L3 77824 S SSDNA OR (SINGL? STRAND? (2N) (DNA OR RNA OR (NUCLE? ACID?)))  
L4 4019 S L2 AND L3  
L5 603 S L2 (5N) L3  
L6 474 S L2 (3N) L3  
L7 26 S L6 AND M13  
L8 15 DUP REM L7 (11 DUPLICATES REMOVED)  
L9 123487 S ANTISENSE? OR (COMPLEM? (2N) (OLIGO? OR NUCLE?))  
L10 126636 S ANTISENSE? OR (ANTI (N) SENSE) OR (COMPLEM? (2N) (OLIGO? OR N  
L11 231 S L10 AND M13  
L12 1 S L10 (2N) M 13  
L13 9 S L10 (2N) M13  
L14 6 DUP REM L13 (3 DUPLICATES REMOVED)  
L15 2854 S L3 AND M13  
L16 69 S L15 AND L10  
L17 1 S L16 AND (CIRC? (5N) L10)  
L18 186 S (CIRC? (5N) L10)  
L19 3 S L18 AND M13  
L20 3 DUP REM L19 (0 DUPLICATES REMOVED)  
L21 35781 S PARK, J?/AU  
L22 800 S MOON, I?/AU  
L23 8 S (L21 OR L22) AND M13  
L24 5 DUP REM L23 (3 DUPLICATES REMOVED)

=> s 124 and 110  
L25 5 L24 AND L10

=> d 125 ibib abs 1-5

L25 ANSWER 1 OF 5 MEDLINE  
ACCESSION NUMBER: 91332994 MEDLINE  
DOCUMENT NUMBER: 91332994 PubMed ID: 1714513  
TITLE: Deletions in the tRNA(Lys) primer-binding site of human  
immunodeficiency virus type 1 identify essential regions  
for reverse transcription.  
AUTHOR: Rhim H; **Park J**; Morrow C D  
CORPORATE SOURCE: Department of Microbiology, University of Alabama,  
Birmingham 35294.  
CONTRACT NUMBER: AI-27767 (NIAID)  
AI27290 (NIAID)  
SOURCE: JOURNAL OF VIROLOGY, (1991 Sep) 65 (9) 4555-64.  
Journal code: 0113724. ISSN: 0022-538X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; AIDS  
ENTRY MONTH: 199109  
ENTRY DATE: Entered STN: 19911006  
Last Updated on STN: 19970203  
Entered Medline: 19910919  
AB The initiation of human immunodeficiency virus type 1 (HIV-1) reverse

transcription occurs by the extension of a tRNA primer bound near the 5' end of the genomic RNA at a position termed the primer-binding site (PBS). The PBS is an 18-nucleotide region of the HIV-1 genome complementary to cellular tRNA(Lys). To further investigate the sequence requirements for the PBS in reverse transcription, deletions in the PBS were created and subcloned into a plasmid containing the infectious HIV-1 proviral genome. The mutations deleted the entire PBS (delta PBS) or the first 9 (delta 1-9), the second 9 (delta 10-18), or 12 (delta 7-18) nucleotides of the PBS. An additional mutation in the PBS was created in which the second nine nucleotides were deleted and nine additional nucleotides were substituted [Lys(1-9)]. The transfection of plasmids containing the wild-type or mutant proviral genomes into tissue culture cells resulted in expression of the HIV-1 gag and env gene products, as determined by immunoprecipitation using sera from AIDS patients. HIV-1 virus was released from the transfected cells, as determined by analysis of the supernatants for reverse transcriptase activity. The infectivity of the viruses derived from the transfection was examined by coculture experiments with SupT1 cells, which support high-level replication of HIV-1. The transfection of plasmids containing HIV-1 proviral genomes with the delta PBS and PBS (delta 1-9) mutations did not produce infectious virus. In contrast, the HIV-1 proviral genomes with the delta 10-18, delta 7-18, and Lys(1-9) mutations in the PBS produced infectious virus upon transfection, although the kinetics of appearance was significantly delayed for the mutant viruses compared with the wild type. To further explore the nature of this defect, the PBS region from integrated proviral genomes was amplified by polymerase chain reaction and individual DNA products were subcloned into M13mp19, followed by a sequence analysis of the PBS region from individual M13 phage clones. In each of the PBS regions examined, the 18-nucleotide PBS complementary to tRNA(Lys) was present. However, nucleotide deletions and insertions were found 3' to the PBS from the samples derived from the transfection of plasmids containing mutant proviral genomes. Upon reinfection, the revertant viruses maintained the deletions 3' to the PBS and had kinetics of replication similar to that of the wild-type virus. (ABSTRACT TRUNCATED AT 400 WORDS)

L25 ANSWER 2 OF 5 CA COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 137:380940 CA  
 TITLE: Unigene unidirectional **antisense** library  
 derived from recombinant bacteriophage or phagemid  
 vector for therapy and massive functional genomics  
 INVENTOR(S): **Park, Jong-Gu; Moon, Ik-Jae; Lee,**  
 Yun-Han  
 PATENT ASSIGNEE(S): Welgene Pharmaceuticals, Inc., S. Korea  
 SOURCE: PCT Int. Appl., 79 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2002092807  | A1   | 20021121 | WO 2002-IB1753  | 20020516 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,<br>GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,<br>LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,<br>PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,<br>UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,<br>TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, |      |          |                 |          |

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
PRIORITY APPLN. INFO.: KR 2001-27071 A 20010517

AB The present invention provides a high throughput system for functional genomics using a unigene **antisense** library comprising large circular (LC)-**antisense** compds. The said large circular (LC)-**antisense** compds are derived from recombinant bacteriophage or phagemid vector. The **antisense** compds. were specific and effective for the elimination of target mRNA. Thus, the system of the present invention is used as temporary knock-down system to unveil functions of genes crit. for diseases. The system of the present invention can be adopted not only for functional genomics but also for effectively validating target for **antisense** or other mol. therapeutics against various malignancies, infections, and other diseases by blocking specific genes involved in the disease.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 5 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 137:364368 CA

TITLE: Libraries of RNAs that can be prepared as large circular molecules and their use in high throughput screening and functional genomics

INVENTOR(S): Park, Jong-Gu; Moon, Ik-Jae; Lee, Yun-Han

PATENT ASSIGNEE(S): Welgene, Inc., S. Korea

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 2002092808 | A1   | 20021121 | WO 2002-IB735   | 20020309 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |

PRIORITY APPLN. INFO.: KR 2001-27071 A 20010517

AB The present invention provides a high-throughput system for functional genomics using a random gene unidirectional **antisense** library comprising large circular RNAs including on or more an **antisense** segments. The **antisense** RNAs are specific and effective inhibitors of translation of a target mRNA. Thus, the system may be effectively used as temporary knock-down system to unveil functions of genes crit. for diseases. The RNA sequences are obtained from a specific biol. state, such as a disease state, by methods such as subtractive hybridization. The selected sequences may then be used to selectively inhibit state-specific genes. These large sequences are generated from bacteriophage or phagemid clones and because they may be several hundred or thousand base pairs long, they are accurate and specific in their effects. Use of bacteriophage M13 and phagemids to generate large circular RNAs inhibiting expression of genes for tumor necrosis factor .alpha. and NF-.kappa.B is demonstrated. The system of the present



invention can be adapted not only for functional genomics but also for effectively validating target for **antisense** or other mol. therapeutics against various malignancies, infections, and other diseases by blocking specific genes involved in the disease.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 5 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 137:227643 CA

TITLE: Large circular target-specific **antisense** nucleic acids for inhibition of gene expression and therapy

INVENTOR(S): **Park, Jong-gu**; Huh, Bin

PATENT ASSIGNEE(S): Welgene Inc., S. Korea

SOURCE: Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 1239034  | A2   | 20020911 | EP 2002-4933    | 20020305 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR |      |          |                 |          |
| US 2002182181   | A1   | 20021205 | US 2002-66498   | 20020130 |
| AU 2002018831   | A5   | 20020912 | AU 2002-18831   | 20020228 |
| CN 1374316  | A    | 20021016 | CN 2002-107110  | 20020308 |
| US 2002168631   | A1   | 20021114 | US 2002-94183   | 20020308 |

PRIORITY APPLN. INFO.: KR 2001-12061 A 20010308  
WO 2001-KR1730 A 20011013

AB The present application describes a large circular target-specific **antisense** mol. that is effective in ablating RNA and protein expression. The large circular **antisense** mol. is used to treat any human disease in which modulation of gene expression can be beneficial to intervene in the disease initiation and progression. Thus, large circular nucleic acid mols. were constructed employing a phagemid vector and the M13KO7 helper bacteriophages contg. the **antisense** sequence for TNF-.alpha., NF-.kappa.B, c-myc, c-myb, c-Ki-ras, and cdk2. TNF.alpha.-M13AS was tested for its circular structure and stability to nucleases. The **antisense** mols. specifically reduced expression of their resp. mRNA, and inhibited growth of cancer cells.

L25 ANSWER 5 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 91:465703 SCISEARCH

THE GENUINE ARTICLE: GB018

TITLE: DELETIONS IN THE TRANSFER-RNALYS PRIMER-BINDING SITE OF HUMAN-IMMUNODEFICIENCY-VIRUS TYPE-1 IDENTIFY ESSENTIAL REGIONS FOR REVERSE TRANSCRIPTION

AUTHOR: RHIM H; **PARK J**; MORROW C D (Reprint)

CORPORATE SOURCE: UNIV ALABAMA, DEPT MICROBIOL, BIRMINGHAM, AL, 35294

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF VIROLOGY, (1991) Vol. 65, No. 9, pp. 4555-4564.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 38

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The initiation of human immunodeficiency virus type 1 (HIV-1) reverse transcription occurs by the extension of a tRNA primer bound near the 5' end of the genomic RNA at a position termed the primer-binding site (PBS).

The PBS is an 18-nucleotide region of the HIV-1 genome complementary to cellular tRNA(Lys). To further investigate the sequence requirements for the PBS in reverse transcription, deletions in the PBS were created and subcloned into a plasmid containing the infectious HIV-1 proviral genome. The mutations deleted the entire PBS (DELTA-PBS) or the first 9 (DELTA-1-9), the second 9 (DELTA-10-18), or 12 (DELTA-7-18) nucleotides of the PBS. An additional mutation in the PBS was created in which the second nine nucleotides were deleted and nine additional nucleotides were substituted [Lys(1-9)]. The transfection of plasmids containing the wild-type or mutant proviral genomes into tissue culture cells resulted in expression of the HIV-1 gag and env gene products, as determined by immunoprecipitation using sera from AIDS patients. HIV-1 virus was released from the transfected cells, as determined by analysis of the supernatants for reverse transcriptase activity. The infectivity of the viruses derived from the transfection was examined by coculture experiments with SupT1 cells, which support high-level replication of HIV-1. The transfection of plasmids containing HIV-1 proviral genomes with the DELTA-PBS and PBS (DELTA-1-9) mutations did not produce infectious virus. In contrast, the HIV-1 proviral genomes with the DELTA-10-18, DELTA-7-18, and Lys(1-9) mutations in the PBS produced infectious virus upon transfection, although the kinetics of appearance was significantly delayed for the mutant viruses compared with the wild-type. To further explore the nature of this defect, the PBS region from integrated proviral genomes was amplified by polymerase chain reaction and individual DNA products were subcloned into M13mp19, followed by a sequence analysis of the PBS region from individual M13 phage clones. In each of the PBS regions examined, the 18-nucleotide PBS complementary to tRNA(Lys) was present. However, nucleotide deletions and insertions were found 3' to the PBS from the samples derived from the transfection of plasmids containing mutant proviral genomes. Upon reinfection, the revertant viruses maintained the deletions 3' to the PBS and had kinetics of replication similar to that of the wild-type virus. These results demonstrate a minimum requirement for the PBS sequence as well as the important role of cellular tRNA(Lys) in the regeneration of the PBS during HIV-1 reverse transcription.

=> d his

(FILE 'HOME' ENTERED AT 13:02:29 ON 26 MAY 2003)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 13:02:49 ON 26 MAY 2003

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L1      101549 S ANTISENSE OR (COMPLE (2N) (OLIGO? OR NUCLEI?))
L2      217407 S ANTISENSE? OR (COMPLE? (2N) (OLIGO? OR NUCLE?))
L3      77824 S SSDNA OR (SINGL? STRAND? (2N) (DNA OR RNA OR (NUCLE? ACID?)))
L4      4019 S L2 AND L3
L5      603 S L2 (5N) L3
L6      474 S L2 (3N) L3
L7      26 S L6 AND M13
L8      15 DUP REM L7 (11 DUPLICATES REMOVED)
L9      123487 S ANTISENSE? OR (COMPLEM? (2N) (OLIGO? OR NUCLE?))
L10     126636 S ANTISENSE? OR (ANTI (N) SENSE) OR (COMPLEM? (2N) (OLIGO? OR N
L11     231 S L10 AND M13
L12     1 S L10 (2N) M 13
L13     9 S L10 (2N) M13
L14     6 DUP REM L13 (3 DUPLICATES REMOVED)
L15     2854 S L3 AND M13
L16     69 S L15 AND L10
L17     1 S L16 AND (CIRC? (5N) L10)
L18     186 S (CIRC? (5N) L10)
L19     3 S L18 AND M13

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L20 3 DUP REM L19 (0 DUPLICATES REMOVED)  
L21 35781 S PARK, J?/AU  
L22 800 S MOON, I?/AU  
L23 8 S (L21 OR L22) AND M13  
L24 5 DUP REM L23 (3 DUPLICATES REMOVED)  
L25 5 S L24 AND L10

=> s l10 and l3

L26 2131 L10 AND L3

=> s l26 and circ?

L27 209 L26 AND CIRC?

=> dup rem l27

PROCESSING COMPLETED FOR L27

L28 114 DUP REM L27 (95 DUPLICATES REMOVED)

=> sl 28 and py<=2001

SL IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> s l28 and py<=2001

2 FILES SEARCHED...

L29 99 L28 AND PY<=2001

=> s l29 and (l10 (w) circ?)

L30 0 L29 AND (L10 (W) CIRC?)

=> s l29 and (l10 (s) circ?)

L31 28 L29 AND (L10 (S) CIRC?)

=> d l31 1-28 ibib abs

L31 ANSWER 1 OF 28 MEDLINE

ACCESSION NUMBER: 1999115548 MEDLINE

DOCUMENT NUMBER: 99115548 PubMed ID: 9916082

TITLE: The R-type pyocin of Pseudomonas aeruginosa C is a  
bacteriophage tail-like particle that contains  
**single-stranded DNA.**

AUTHOR: Lee F K; Dudas K C; Hanson J A; Nelson M B; LoVerde P T;  
Apicella M A

CORPORATE SOURCE: Department of Microbiology, College of Medicine, University  
of Iowa, Iowa City, Iowa, USA.

CONTRACT NUMBER: AI 18384 (NIAID)

SOURCE: INFECTION AND IMMUNITY, (1999 Feb) 67 (2) 717-25.  
Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-L06240

ENTRY MONTH: 199903

ENTRY DATE: Entered STN: 19990324

Last Updated on STN: 19990324

Entered Medline: 19990309

AB Pseudomonas aeruginosa R-type pyocin particles have been described as  
bacteriocins that resemble bacteriophage tail-like structures. Because of  
their unusual structure, we reexamined whether they contained nucleic  
acids. Our data indicated that pyocin particles isolated from P.  
aeruginosa C (pyocin C) contain DNA. Probes generated from this DNA by

the random-primer extension method hybridized to distinct bands in restriction endonuclease-digested *P. aeruginosa* C genomic DNA. These probes also hybridized to genomic DNA from 6 of 18 *P. aeruginosa* strains that produced R-type pyocins. Asymmetric PCR, **complementary oligonucleotide** hybridization, and electron microscopy indicated that pyocin C particles contained closed **circular single-stranded DNA**, approximately 4.0 kb in length. Examination of total intracellular DNA from mitomycin C-induced cultures revealed the presence of two extrachromosomal DNA molecules, a double-stranded molecule and a single-stranded molecule, which hybridized to pyocin DNA. Sequence analysis of 7,480 nucleotides of *P. aeruginosa* C chromosomal DNA containing the pyocin DNA indicated the presence of pyocin open reading frames with similarities to open reading frames from filamentous phages and cryptic phage elements. We did not observe any similarities to known phage structural proteins or previously characterized pseudomonas prt genes expressing R-type pyocin structural proteins. These studies demonstrate that pyocin particles from *P. aeruginosa* C are defective phages that contain a novel closed **circular single-stranded DNA** and that this DNA was derived from the chromosome of *P. aeruginosa* C.

L31 ANSWER 2 OF 28 MEDLINE  
 ACCESSION NUMBER: 1998440432 MEDLINE  
 DOCUMENT NUMBER: 98440432 PubMed ID: 9765572  
 TITLE: Methanococcus jannaschii flap endonuclease: expression, purification, and substrate requirements.  
 AUTHOR: Rao H G; Rosenfeld A; Wetmur J G  
 CORPORATE SOURCE: Department of Microbiology, Mount Sinai School of Medicine, New York, New York 10029, USA.  
 CONTRACT NUMBER: HG01356 (NHGRI)  
 SOURCE: JOURNAL OF BACTERIOLOGY, (1998 Oct) 180 (20) 5406-12.  
 Journal code: 2985120R. ISSN: 0021-9193.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199810  
 ENTRY DATE: Entered STN: 19990106  
 Last Updated on STN: 20000303  
 Entered Medline: 19981030

AB The flap endonuclease (FEN) of the hyperthermophilic archaeon *Methanococcus jannaschii* was expressed in *Escherichia coli* and purified to homogeneity. FEN retained activity after preincubation at 95 degrees C+ for 15 min. A pseudo-Y-shaped substrate was formed by hybridization of two partially **complementary oligonucleotides**. FEN cleaved the strand with the free 5' end adjacent to the single-strand-duplex junction. Deletion of the free 3' end prevented cleavage. Hybridization of a **complementary oligonucleotide** to the free 3' end moved the cleavage site by 1 to 2 nucleotides. Hybridization of excess **complementary oligonucleotide** to the free 5' end failed to block cleavage, although this substrate was refractory to cleavage by the 5'-3' exonuclease activity of Taq DNA polymerase. For verification, the free 5' end was replaced by an internally labeled hairpin structure. This structure was a substrate for FEN but became a substrate for Taq DNA polymerase only after exonucleolytic cleavage had destabilized the hairpin. A **circular** duplex substrate with a 5' single-stranded branch was formed by primer extension of a partially **complementary oligonucleotide** on virion phiX174. This denaturation-resistant substrate was used to examine the effects of temperature and solution properties, such as pH, salt, and divalent ion concentration on the

turnover number of the enzyme.

L31 ANSWER 3 OF 28 MEDLINE  
ACCESSION NUMBER: 1998267209 MEDLINE  
DOCUMENT NUMBER: 98267209 PubMed ID: 9602151  
TITLE: Amplification of target-specific, ligation-dependent  
**circular** probe.  
AUTHOR: Zhang D Y; Brandwein M; Hsuih T C; Li H  
CORPORATE SOURCE: The Lillian, Henry M. Stratton-Hans Popper Department of  
Pathology, Department of Otolaryngology, Mount Sinai School  
of Medicine, New York, NY 10029, USA..  
david\_zhang@smtplink.mssm.edu  
SOURCE: GENE, (1998 May 12) 211 (2) 277-85.  
Journal code: 7706761. ISSN: 0378-1119. *Maybe*  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199807  
ENTRY DATE: Entered STN: 19980723  
Last Updated on STN: 19980723  
Entered Medline: 19980714

AB We describe a novel polymerase chain reaction (PCR)-based gene  
amplification method utilizing a **circularizable**  
oligodeoxyribonucleotide probe (C-probe). The C-probe contains two target  
complementary regions located at each terminus and an interposed generic  
PCR primer binding region. The hybridization of C-probe to a target  
brings two termini in direct apposition as the complementary regions of  
C-probe wind around the target to form a double helix. Subsequent  
ligation of the two termini results in a covalently linked C-probe that  
becomes 'locked on to' the target. The **circular** nature of the  
C-probe allows for the generation of a multimeric **single-**  
**stranded DNA (ssDNA)** via extension of the  
**antisense** primer by Taq DNA polymerase along the C-probe and  
displacement of downstream strand, analogous to 'rolling **circle**'  
replication of bacteriophage in vivo. This multimeric **ssDNA**  
then serves as a template for multiple sense primers to hybridize, extend,  
and displace downstream DNA, generating a large ramified (branching) DNA  
complex. Subsequent thermocycling denatures the dsDNA and initiates the  
next round of primer extension and ramification. This model results in  
significantly improved amplification kinetics (super-exponential) as  
compared to conventional PCR. Our results show that the C-probe was 1000  
times more sensitive than the corresponding linear hemiprobe for  
detecting Epstein-Barr virus early RNA. The C-probe not only increases  
the power of amplification but also offers a means for decontaminating  
carryover amplicons. As the ligated C-probes possess no free termini,  
they are resistant to exonuclease digestion, whereas contaminated linear  
amplicons are susceptible to digestion. Treatment of the ligation  
reaction mixture with exonuclease prior to amplification eliminated the  
amplicon contaminant, which could also have been co-amplified with the  
same PCR primers; only the ligated C-probes were amplified. The combined  
advantages of the C-probe and thermocycling have a broad applicability for  
the detection of both DNA and RNA. Finally, we described a novel  
isothermal amplification method, ramification extension amplification,  
utilizing **circular** nature of C-probe and displacement activity  
of DNA polymerase.

L31 ANSWER 4 OF 28 MEDLINE  
ACCESSION NUMBER: 1998167937 MEDLINE  
DOCUMENT NUMBER: 98167937 PubMed ID: 9500923  
TITLE: The beta protein of phage lambda promotes strand exchange.  
AUTHOR: Li Z; Karakousis G; Chiu S K; Reddy G; Radding C M

CORPORATE SOURCE: Department of Genetics, Yale University School of Medicine,  
New Haven, CT 06510, USA.

CONTRACT NUMBER: PO1 CA39238 (NCI)  
R37 GM33504 (NIGMS)

SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1998 Mar 6) 276  
(4) 733-44.  
Journal code: 2985088R. ISSN: 0022-2836.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199805

ENTRY DATE: Entered STN: 19980514  
Last Updated on STN: 20000303  
Entered Medline: 19980504

AB Bacteriophage lambda encodes a 28 kDa protein called beta that binds to **single-stranded DNA** and promotes the renaturation of complementary single strands. beta Protein fails to bind directly to duplex DNA but remains bound to the DNA product of renaturation that beta itself catalyzes. These observations led to an examination of the ability of beta protein to promote strand exchange. beta Protein caused the replacement of a 43-mer oligonucleotide annealed to M13 **circular single-stranded DNA** by a homologous 63-mer whose 20 extra **nucleotide** residues were **complementary** to the adjacent 3' region of M13 DNA. The role of beta protein in this reaction was manifested in several ways: beta protein pushed the exchange through four to eight mismatches, which blocked exchange mediated by spontaneous renaturation and branch migration; beta imposed a polarity on the strand exchange that was lacking in the spontaneous reaction; and beta remained bound to the heteroduplex product of strand exchange. These observations reveal a mechanism by which a protein can drive strand exchange in one direction without using ATP or any other exogenous source of energy.  
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L31 ANSWER 5 OF 28 MEDLINE

ACCESSION NUMBER: 1998060892 MEDLINE

DOCUMENT NUMBER: 98060892 PubMed ID: 9396802

TITLE: Inhibitory properties of double-helix-forming **circular** oligonucleotides.

AUTHOR: Azhayeva E; Azhayev A; Auriola S; Tengvall U; Urtti A; Lonnberg

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kuopio, FIN-70211 Kuopio, Finland.

SOURCE: NUCLEIC ACIDS RESEARCH, (1997 Dec 15) 25 (24) 4954-61.  
Journal code: 0411011. ISSN: 0305-1048.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199802

ENTRY DATE: Entered STN: 19980306  
Last Updated on STN: 19980306  
Entered Medline: 19980224

AB Several **circular** oligonucleotides were synthesized and characterized by electrospray ionization mass spectrometry. Experiments on termination of primer extension catalysed by DNA polymerases, Klenow fragment and Tth have demonstrated that a double helix forming **circular** 2'-deoxyribooligomer containing a 25mer sequence complementary to the target **single-stranded DNA** along with a 34mer random mismatching stretch appears to be a

potent inhibitor of replication in vitro. Studies on inhibition of luciferase gene expression in a cell-free transcription-translation system have shown that a duplex forming **circular** 2'-deoxyribooligonucleotide containing a 25mer sequence complementary to the target mRNA and a 14mer random mismatching stretch can serve as an effective **antisense** compound as a standard linear **complementary oligomer**. Features of double helix forming **circular** oligonucleotides composed of 2'-deoxyribonucleosides seem to be useful for the design of new antigene and **antisense** agents.

L31 ANSWER 6 OF 28 MEDLINE  
 ACCESSION NUMBER: 94252981 MEDLINE  
 DOCUMENT NUMBER: 94252981 PubMed ID: 8195068  
 TITLE: Characterization of a region of plasmid pBL1 of Brevibacterium lactofermentum involved in replication via the rolling **circle** model.  
 AUTHOR: Fernandez-Gonzalez C; Cadenas R F; Noirot-Gros M F; Martin J F; Gil J A  
 CORPORATE SOURCE: Section of Microbiology, Faculty of Biology, University of Leon, Spain.  
 SOURCE: JOURNAL OF BACTERIOLOGY, (1994 Jun) 176 (11) 3154-61.  
 Journal code: 2985120R. ISSN: 0021-9193.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199406  
 ENTRY DATE: Entered STN: 19940707  
 Last Updated on STN: 19940707  
 Entered Medline: 19940630

AB The minimal region for autonomous replication of pBL1, a 4.5-kb cryptic plasmid of Brevibacterium lactofermentum ATCC 13869 that has been used to construct a variety of corynebacterium vectors, was shown to be contained on a 1.8-kb HindIII-SphI DNA fragment. This region contains two open reading frames (ORFs) (ORF1 and ORF5) which are essential for pBL1 replication in B. lactofermentum. Accumulation of single-strand intermediates in some of the constructions indicates that plasmid pBL1 replicates via the rolling **circle** replication model; its plus strand and minus strand were identified by hybridization with two synthetic **oligonucleotide** probes **complementary** to each pBL1 strand. ORF1 seems to encode the Rep protein and showed partial homology with sequences for Rep proteins from Streptomyces plasmids which replicate via rolling **circle** replication such as pIJ101, pSB24, and pJV1.

L31 ANSWER 7 OF 28 MEDLINE  
 ACCESSION NUMBER: 89301133 MEDLINE  
 DOCUMENT NUMBER: 89301133 PubMed ID: 2662813  
 TITLE: Oligodeoxynucleotide-directed cleavage and repair of a single-stranded vector: a method of site-specific mutagenesis.  
 AUTHOR: Zhu D L  
 CORPORATE SOURCE: Institut Jacques Monod, CNRS, Paris, France.  
 SOURCE: ANALYTICAL BIOCHEMISTRY, (1989 Feb 15) 177 (1) 120-4.  
 Journal code: 0370535. ISSN: 0003-2697.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals

ENTRY MONTH: 198908  
ENTRY DATE: Entered STN: 19900309  
Last Updated on STN: 19900309  
Entered Medline: 19890810

AB A simple and efficient site-specific mutagenesis method is described. First, a single-stranded (ss) **circular** vector is linearized at the site where the desired mutation will be introduced. To do this, an **oligodeoxynucleotide complementary** to the target region of the ss vector and containing a restriction enzyme recognition sequence is annealed to the **circular** ss vector, and the partial double-strand formed is subsequently cleaved with that enzyme. Then, another oligodeoxynucleotide spanning the nick and carrying the mutation is annealed to the linearized ss DNA template and the annealed mixture is used directly to transform Escherichia coli without prior enzymatic DNA synthesis in vitro. The procedure has been applied successfully to constructing insertion, deletion, and point mutations in both M13 phage vectors and plasmid vectors containing the fl origin of replication.

L31 ANSWER 8 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1995:341946 BIOSIS

DOCUMENT NUMBER: PREV199598356246

TITLE: Properties and anti-HIV activity of **circular** sense and **antisense** oligonucleotides.

AUTHOR(S): Yamakawa, Hidefumi; Ishibashi, Toshiaki; Nakashima, Hideki; Yamamoto, Naoki; Takai, Kazuyuki; Takaku, Hiroshi (1)

CORPORATE SOURCE: (1) Rational Drug Design Lab., Misato, Matsukawa, Fukushima, Fukushima 960-12 Japan

SOURCE: Nucleosides & Nucleotides, (1995) Vol. 14, No. 3-5, pp. 1149-1152.

ISSN: 0732-8311.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The **circularization** of a 48 mer oligonucleotide was investigated by using enzymatic ligation with T4 DNA ligase. This method yielded 30% **circular** molecules. The **circular** oligonucleotides are molecules with no free ends and are therefore more resistant to exonuclease attack. The **circular** oligonucleotide has remarkably increased Tm values as compared to the nicked and double stranded DNAs. However, the RNase H activity is lower than that with a **single stranded DNA**. We also describe the anti-HIV activity of a **circular** oligonucleotide.

L31 ANSWER 9 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1994:251391 BIOSIS

DOCUMENT NUMBER: PREV199497264391

TITLE: Base pairing and steric interactions between pyrimidine strand bridging loops and the purine strand in DNA pyrimidine-purine-pyrimidine triplexes.

AUTHOR(S): Booher, Mark A.; Wang, Shaohui; Kool, Eric T. (1)

CORPORATE SOURCE: (1) Dep. Chem., Univ. Rochester, Rochester, NY 14627 USA

SOURCE: Biochemistry, (1994) Vol. 33, No. 15, pp. 4645-4651.

ISSN: 0006-2960.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Bimolecular triple-helical DNA complexes recently have found use in a new strategy for the recognition of **single-stranded nucleic acids**, in which **circular** (Kool, 1991; Prakash & Kool, 1992) or hairpin-shaped (Giovannangeli et al., 1991; D'Souza & Kool, 1992) oligonucleotides bind these single strands by triplex formation. Bimolecular triplexes may also be formed in vivo as H-DNA, where this structure may potentially play a role in gene expression and recombination (Belotserkovskii et al., 1990; Hanvey et al., 1989;



Shimizu et al., 1989). In all of these complexes, the central strand of the triplex must pass beyond the loop that bridges the outer two strands, and models and preliminary experiments have indicated that there may be important interactions between this central strand and the loop (Prakash & Kool, 1992). We now report thermal denaturation studies carried out specifically to investigate these interactions in detail, using as a model the 5'-loop and 3'-loop complexes formed between 14 pyrimidine oligodeoxynucleotides having the sequence 5'-dTCTTTTCL-1TTTL-5CTTTTCTT, where L-1 and L-5 represent varied nucleotides in the loop (which is underlined), and eight target strands having the sequence 5'-dCCCCCFAAGAAAAG-3' or 5'-dGAAAAGAAFCFFFF-3', where F is a varied nucleotide flanking the triplex in the central strand. Results correlated from 64 different sequence combinations show that there is wide variation in the stabilities of the complexes, indicating specific and substantial interactions between the nucleotides at the L-1, F, and L-5 positions. Melting temperatures at pH 7.0 range from 17.0 degree C to 34.6 degree C and free energies (37 degree C) range from -3.2 to -7.8 kcal mol<sup>-1</sup>. Several general conclusions are drawn from the 64 combinations studied: (1) Extra stability is gained when one of the first (L-1) or fifth (L-5) nucleotides in the loop is complementary to the F nucleotide in the purine strand, with an average advantage of 1.9-3.0 degree C in T-m and 0.6 kcal in free energy. (2) Even higher stability is gained when both the L-1 and L-5 nucleotides are complementary to the flanking F nucleotide. The advantage (relative to no complementarity) is 3.2-4.7 degree C in T-m and 1.1-1.5 kcal in free energy, on average; however, evidence indicates that this interaction is not the result of standard triple-helix pairing. (3) The correct choice of loop nucleotides can add both binding affinity and sequence selectivity to bimolecular triplexes. Binding studies of two circular oligodeoxynucleotides constructed as a test of the loop studies shows that the results allow semiquantitative predictions of the stabilities of bimolecular triplexes that involve these loop interactions. In the design of synthetic oligonucleotides as triplex-forming agents, the results suggest optimal choices of loop nucleotides for binding a given target sequence. The results may also aid in the understanding of the relative stabilities of H-DNA complexes.

L31 ANSWER 10 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 1993:432235 BIOSIS  
 DOCUMENT NUMBER: PREV199396086860  
 TITLE: Analysis of replication of HIV-1 by mutagenesis of reverse transcriptase and nucleocapsid protein.  
 AUTHOR(S): Moelling, Karein (1); Volkmann, Silke (1); Dannull, Jens (1); Surovoy, Andrej; Jung, Gunter  
 CORPORATE SOURCE: (1) Max-Planck-Inst. Molekulare Genetik, Abt. Schuster, Ihnestrassse 73, W-1000 Berlin 33 Germany  
 SOURCE: AIDS-Forschung, (1993) Vol. 8, No. 5, pp. 243-248.  
 ISSN: 0179-3098.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English; German

AB Replication of retroviral RNA into double-stranded DNA involves RNA-dependent, DNA-dependent DNA synthesis by reverse transcriptase (RT) and hydrolysis of RNA-DNA hybrids by action of the RNase H. Both enzyme activities are coupled and cooperate. Among all 14 known RT sequences 7 amino acids are highly conserved in the RNase H domain. Three of these have been mutagenized and their properties studied in vitro, aminoacid residue glutamine 475 to glutamate (Q475E), asparagine 495 to aspartate and histidine 539 to glutamine (H539N). One of the mutants does not recognize the polypurine tract, PPT, the primer for plus-strand DNA synthesis, a defect which makes this mutant noninfectious. Based on this observation, the PPT is under investigation as target for anti-

sense or triple helix forming (TFO) DNA oligonucleotides in order to prevent retroviral replication. Furthermore, the nucleocapsid protein p7 (NCp7) protein has been analyzed. It binds to **single-stranded** (ss) **RNA**, **ssDNA** and double-stranded (ds) DNA in vitro. Modification of its zinc-finger structures affects binding to **ssDNA** but not to RNA and dsDNA. The NCp7 causes a slight stimulation of RNA-dependent DNA-synthesis by the RT in vitro. Furthermore, the conformation of NCp7 has been determined by **circular** dichroism (CD).

L31 ANSWER 11 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1980:159341 BIOSIS

DOCUMENT NUMBER: BA69:34337

TITLE: HEPATITIS B VIRAL DNA MOLECULES HAVE COHESIVE ENDS.

AUTHOR(S): SATTTLER F; ROBINSON W S

CORPORATE SOURCE: DEP. MED., STANFORD UNIV. SCH. MED., STANFORD, CALIF. 94305, USA.

SOURCE: J VIROL, (1979) 32 (1), 226-232.

CODEN: JOVIAM. ISSN: 0022-538X.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Hepatitis B virus DNA made fully double stranded by a virion DNA polymerase reaction could be converted from **circular** to linear molecules by heating in 10 mM NaCl at 77.degree. C or in 100 mM NaCl at 90.degree. C for 15 min. Heat-generated linear hepatitis B virus DNA was reannealed to **circular** molecules by incubating in higher salt concentrations. The identity of the molecular forms was established by their electrophoretic mobility and appearance in electron micrographs. Recircularization was blocked by reacting linear molecules with nuclease S1 or avian myeloblastosis virus reverse transcriptase. The heated linear DNA apparently had **single-stranded** ends with **complementary nucleotide** sequences. A discontinuity or nick is present in each strand of the **circular** DNA molecule after the single-stranded region is made double stranded by the virion DNA polymerase reaction is suggested. The difference in contour length by EM of **circular** and linear molecules spread under aqueous conditions suggested that the discontinuities in the two strands were about 270 base pairs apart. The amount of nucleotide incorporated into the ends of heat-generated linear hepatitis B virus DNA by reverse transcriptase suggested that the single-stranded ends were about 305 bases in length. This fully double-stranded linear DNA was cleaved with EcoRI or HpaI restriction endonuclease. The sum of the 2 fragments generated by each totaled 3510 base pairs, 310 base pairs greater than the contour length of **circular** hepatitis B virus DNA which represents a 3rd estimate of the distance between the discontinuities in the 2 DNA strands of **circular** DNA. Restriction endonuclease cleavage also indicated that the ends of heated linear DNA which correspond to the discontinuities in the 2 strands of the **circular** DNA are at unique sites in the DNA with respect to the restriction sites.

L31 ANSWER 12 OF 28 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001396404 EMBASE

TITLE: Effect of secondary structure on the thermodynamics and kinetics of PNA hybridization to DNA hairpins.

AUTHOR: Kushon S.A.; Jordan J.P.; Seifert J.L.; Nielsen H.; Nielsen P.E.; Armitage B.A.

CORPORATE SOURCE: B.A. Armitage, Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, PA 15213-3890, United States. army@cyrus.andrew.cmu.edu

SOURCE: Journal of the American Chemical Society, (7 Nov 2001) 123/44 (10805-10813).

Refs: 89

ISSN: 0002-7863 CODEN: JACSAT  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The binding of a series of PNA and DNA probes to a group of unusually stable DNA hairpins of the tetraloop motif has been observed using absorbance hypochromicity (ABS), **circular** dichroism (CD), and a colorimetric assay for PNA/DNA duplex detection. These results indicate that both stable PNA-DNA and DNA-DNA duplexes can be formed with these target hairpins, even when the melting temperatures for the resulting duplexes are up to 50.degree.C lower than that of the hairpin target. Both hairpin/single-stranded and hairpin/hairpin interactions are considered in the scope of these studies. Secondary structures in both target and probe molecules are shown to depress the melting temperatures and free energies of the probe-target duplexes. Kinetic analysis of hybridization yields reaction rates that are up to 160-fold slower than hybridization between two unstructured strands. The thermodynamic and kinetic obstacles to hybridization imposed by both target and probe secondary structure are significant concerns for the continued development of **antisense** agents and especially diagnostic probes.

L31 ANSWER 13 OF 28 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000379382 EMBASE  
TITLE: Peptide nucleic acids: Versatile tools for gene therapy strategies.  
AUTHOR: Dean D.A.  
CORPORATE SOURCE: D.A. Dean, Div. Pulmonary/Critical Care Med., Northwestern University, Medical School, 300 E. Superior Ave., Chicago, IL 60611, United States. dean@northwestern.edu  
SOURCE: Advanced Drug Delivery Reviews, (15 Nov 2000) 44/2-3 (81-95).  
Refs: 72  
ISSN: 0169-409X CODEN: ADDREP  
PUBLISHER IDENT.: S 0169-409X(00)00087-9  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 022 Human Genetics  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Peptide nucleic acids, or PNAs, are oligonucleotide analogs in which the phosphodiester backbone is replaced with a polyamide structure. First synthesized less than 10 years ago, they have received great attention due to their several favorable properties, including resistance to nuclease and protease digestion, stability in serum and cell extracts, and their high affinity for RNA and single and double-stranded DNA targets. Although initially designed and demonstrated to function as **antisense** and antigene reagents that inhibit both transcription and translation by steric hindrance, more recent applications have included gene activation by synthetic promoter formation and mutagenesis of chromosomal targets. Most notably for gene delivery, they have been used to specifically label plasmids and act as adapters to link synthetic peptides or ligands to the DNA. Thus, their great potential lies in the ability to attach specific targeting peptides to plasmids to **circumvent** such barriers to gene transfer as cell-targeting or nuclear localization, thereby increasing the efficacy of gene therapy. Copyright (C) 2000 Elsevier Science B.V.

L31 ANSWER 14 OF 28 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94258880 EMBASE

DOCUMENT NUMBER: 1994258880

TITLE: Strand displacement amplification as an in vitro model for rolling-**circle** replication: Deletion formation and evolution during serial transfer.

AUTHOR: Walter N.G.; Strunk G.

CORPORATE SOURCE: Department of Biochemical Kinetics, Max Planck Biophysical Chem. Inst., Am Fassberg 11, D-37077 Gottingen, Germany

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) 91/17 (7937-7941).  
ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Strand displacement amplification is an isothermal DNA amplification reaction based on a restriction endonuclease nicking its recognition site and a polymerase extending the nick at its 3' end, displacing the downstream strand. The reaction resembles rolling-**circle** replication of single-stranded phages and small plasmids. The displaced sense strand serves as target for an **antisense** reaction and vice versa, resulting in exponential growth and the autocatalytic nature of this in vitro reaction as long as the template is the limiting agent. We describe the optimization of strand displacement amplification for in vitro evolution experiments under serial transfer conditions. The reaction was followed and controlled by use of the fluorescent dye thiazole orange binding to the amplified DNA. We were able to maintain exponential growth conditions with a doubling time of 3.0 min throughout 100 transfers or .simeq.350 molecular generations by using an automatic handling device. Homology of in vitro amplification with rolling-**circle** replication was mirrored by the occurring evolutionary processes. Deletion events most likely caused by a slipped mispairing mechanism as postulated for in vivo replication took place. Under our conditions, the mutation rate was high and a molecular quasi-species formed with a mutant lacking internal hairpin formation ability and thus outgrowing all other species under dGTP/dCTP deficiency.

L31 ANSWER 15 OF 28 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 135:29817 CA

TITLE: Generation of **single-strand circular DNA** from two or more hairpin **oligonucleotides** with **complementary** single-strand ends

INVENTOR(S): Abarzua, Patricio

PATENT ASSIGNEE(S): Molecular Staging Inc., USA

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE         |
|---------------|------|----------|-----------------|--------------|
| WO 2001040516 | A2   | 20010607 | WO 2000-US32370 | 20001128 <-- |
| WO 2001040516 | A3   | 20020711 |                 |              |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,  
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2360342 AA 20010607 CA 2000-2360342 20001128 <--  
 EP 1238105 A2 20020911 EP 2000-980827 20001128  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 US 6498023 B1 20021224 US 2000-723685 20001128  
 PRIORITY APPLN. INFO.: US 1999-168511P P 19991202  
 WO 2000-US32370 W 20001128

AB The present invention provides a method for the rapid simultaneous prodn.  
 of a plurality of **single-stranded DNA**  
**circles** having a predetd. size and nucleotide sequence using  
 pre-designed hairpin **oligonucleotides** contg.  
**complementary** sequences for directing ligation to form  
 dumbbell-shaped monomers followed by heat denaturation to yield  
**single-stranded DNA circles**.

L31 ANSWER 16 OF 28 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 133:248497 CA

TITLE: Targeting of **single-stranded**  
**DNA** and **RNA** containing adjacent  
 pyrimidine and purine tracts by triple helix formation  
 with **circular** and clamp oligonucleotides

AUTHOR(S): Maksimenko, Andrei V.; Volkov, Evgueny M.; Bertrand,  
 Jean-Remi; Porumb, Horea; Malvy, Claude; Shabarova,  
 Zoe A.; Gottikh, Marina B.

CORPORATE SOURCE: Belozersky Research Institute of Physico-Chemical  
 Biology and Department of Chemistry, Moscow State  
 University, Russia

SOURCE: European Journal of Biochemistry (2000),  
 267(12), 3592-3603

CODEN: EJBCAI; ISSN: 0014-2956

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this work was to construct an anti-messenger targeted to the  
 pim-1 oncogene transcript, based on **circular** or clamp  
 oligodeoxyribonucleotides. The formation of bimol. triplexes by clamp or  
**circular** oligonucleotides was investigated using single-stranded  
 targets of both DNA (5'-CCCTCCTTTGAAGAA-3') and RNA type  
 (5'-CCCUCUUUGAAGAA-3'). The third, Hoogsteen strand of the triplex was  
 represented by G,T-rich sequences. The secondary structures of the  
 complexes were detd. by thermal denaturation, CD and gel mobility shift  
 expts. and shown to depend on the nature of the target strand. With DNA  
 as target, the sequence of a clamp (or **circular**) oligonucleotide  
 that formed the triple helix was 3'-GGGAGGAACTTCTTTT-TTGTGTTT-TT-GGTGGG-  
 5', where the first TT dinucleotide (in italics) is a linker and the  
 second TT (**bold**) represents the bridge through which the Hoogsteen strand  
 switches from one strand of the Watson-Crick duplex to the other, once the  
 duplex is formed by the corresponding portion of the anti-messenger  
 (underlined). The portion of the Hoogsteen sequence of the triplex  
 between the two TT dinucleotides binds to the 3' extremity of the target  
 strand and runs parallel to it. The portion situated at the 5' end of the  
 oligonucleotide switches to the purine tract of the complementary strand  
 of the duplex and is antiparallel to it. In contrast, with RNA as target,  
 for a branched clamp oligonucleotide that formed a triple helix over its  
 entire length (5'-TTCTTCAAAGGAGGG-3'.cxa.3'-GGGTGGTTT-T-GTTGTT-5') the  
 portion of the Hoogsteen sequence that bound to the 3' extremity of the

target strand had to be antiparallel to it.  
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 28 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 133:145882 CA  
TITLE: **Circular** DNA vectors for synthesis of RNA  
and DNA  
INVENTOR(S): Kool, Eric T.  
PATENT ASSIGNEE(S): University of Rochester, USA  
SOURCE: U.S., 48 pp., Cont.-in-part of U.S. 5,714,320.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE         |
|--|------|----------|-----------------|--------------|
| US 6096880   | A    | 20000801 | US 1997-805631  | 19970226 <-- |
| US 5714320   | A    | 19980203 | US 1995-393439  | 19950223 <-- |
| US 6077668   | A    | 20000620 | US 1997-910632  | 19970813 <-- |
| WO 9838300   | A1   | 19980903 | WO 1998-US3784  | 19980226 <-- |
| W: JP  |      |          |                 |              |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |              |
| EP 977839  | A1   | 20000209 | EP 1998-907649  | 19980226 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI      |      |          |                 |              |
| US 6368802   | B1   | 20020409 | US 2000-569344  | 20000511     |
| US 2003087241  | A1   | 20030508 | US 2001-997931  | 20011130     |
| PRIORITY APPLN. INFO.:   |      |          |                 |              |
|  |      |          | US 1993-47860   | B2 19930415  |
|  |      |          | US 1995-393439  | A2 19950223  |
|  |      |          | US 1997-805631  | A2 19970226  |
|  |      |          | WO 1998-US3784  | W 19980226   |
|  |      |          | US 2000-569344  | A2 20000511  |

AB The present invention provides methods for synthesis, and therapeutic use of DNA and RNA oligonucleotides and analogs. RNA oligonucleotides are synthesized using a small, **circular** DNA template which lacks an RNA polymerase promoter sequence. The RNA synthesis is performed by combining a **circular** single-stranded oligonucleotide template with an effective RNA polymerase and at least two types of ribonucleotide triphosphate to form an RNA oligonucleotide multimer comprising multiple copies of the desired RNA oligonucleotide sequence. Preferably, the RNA oligonucleotide multimer is cleaved to produce RNA oligonucleotides having well-defined ends. Preferred RNA oligonucleotide multimers may contain ribozymes capable of both cis (autolytic) and trans cleavage, **antisense** RNA, or decoy RNA.

REFERENCE COUNT: 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L31 ANSWER 18 OF 28 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 130:48294 CA  
TITLE: Efficient and simpler method to construct normalized  
cDNA libraries with improved representations of  
full-length cDNAs  
INVENTOR(S): Soares, Marcelo Bento; Bonaldo, Mariade Fatima  
PATENT ASSIGNEE(S): The Trustees of Columbia University In the City of New  
York, USA  
SOURCE: U.S., 28 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE         |
|------------|------|----------|-----------------|--------------|
| US 5846721 | A    | 19981208 | US 1996-715941  | 19960919 <-- |

PRIORITY APPLN. INFO.: US 1996-715941 19960919

AB This invention provides a method to normalize a cDNA library comprising:  
(a) constructing a directionally cloned library contg. cDNA inserts wherein the insert is capable of being amplified by polymerase chain reaction; (b) converting a double-stranded cDNA library into **single-stranded DNA circles**; (c) generating **single-stranded nucleic acid mols. complementary to the single-stranded DNA circles** converted in step (b) by polymerase chain reaction with appropriate primers; (d) hybridizing the **single-stranded DNA circles** converted in step (b) with the **complementary single-stranded nucleic acid mols.** generated in step (c) to produce partial duplexes to an appropriate C0t; and (e) sepg. the unhybridized **single-stranded DNA circles** from the hybridized **DNA circles**, thereby generating a normalized cDNA library. This invention also provides a method to normalize a cDNA library wherein the generating of **single-stranded nucleic acid mols. complementary to the single-stranded DNA circles** converted in step (b) is by excising cDNA inserts from the double-stranded cDNA library; purifying the cDNA inserts from cloning vectors; and digesting the cDNA inserts with an exonuclease. This invention further provides a method to construct a subtractive cDNA library following the steps described above. This invention further provides normalized and/or subtractive cDNA libraries generated by the above methods.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 28 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 129:226611 CA  
TITLE: **Circular** DNA vectors for synthesis of RNA and DNA  
INVENTOR(S): Kool, Eric T.  
PATENT ASSIGNEE(S): University of Rochester, USA  
SOURCE: PCT Int. Appl., 101 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE         |
|--|------|----------|-----------------|--------------|
| WO 9838300   | A1   | 19980903 | WO 1998-US3784  | 19980226 <-- |
| W: JP  |      |          |                 |              |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |              |
| US 6096880   | A    | 20000801 | US 1997-805631  | 19970226 <-- |
| EP 977839  | A1   | 20000209 | EP 1998-907649  | 19980226 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI      |      |          |                 |              |

PRIORITY APPLN. INFO.: US 1997-805631 A 19970226  
US 1993-47860 B2 19930415  
US 1995-393439 A2 19950223  
WO 1998-US3784 W 19980226

AB The present invention provides methods for synthesis and therapeutic use

of DNA and RNA oligonucleotides and analogs. RNA oligonucleotides are synthesized using a small, **circular** DNA template which lacks an RNA polymerase promoter sequence. The RNA synthesis is performed by combining a **circular** single-stranded oligonucleotide template with an effective RNA polymerase and at least two types of ribonucleotide triphosphate to form an RNA oligonucleotide multimer comprising multiple copies of the desired RNA oligonucleotide sequence. Preferably, the RNA oligonucleotide multimer is cleaved to produce RNA oligonucleotides having well-defined ends. Preferred RNA oligonucleotide multimers may contain ribozymes capable of both cis (autolytic) and trans cleavage, **antisense** RNA, or decoy RNA.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 28 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 128:98540 CA

TITLE: Procedure for normalization of cDNA libraries

INVENTOR(S): Bonaldo, Maria Defatima; Soares, Marcelo Bento

PATENT ASSIGNEE(S): Trustees of Columbia University In the City of New York, USA

SOURCE: U.S., 8 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE         |
|------------------------|------|----------|-----------------|--------------|
| US 5702898             | A    | 19971230 | US 1995-465857  | 19950606 <-- |
| PRIORITY APPLN. INFO.: |      |          | US 1995-465857  | 19950606     |

AB This invention provides a method to normalize a cDNA library constructed in a vector capable of being converted to single-stranded **circles** and capable of producing **complementary nucleic acid** mols. to the single-stranded **circles** comprising: (a) converting the cDNA library in single-stranded **circles**; (b) generating **complementary nucleic acid** mols. to the single-stranded **circles**; (c) hybridizing the single-stranded **circles** converted in step (a) with **complementary nucleic acid** mols. of step (b) to produce partial duplexes to an appropriate Cot; (e) sepg. the unhybridized single-stranded **circles** from the hybridized single-stranded **circles**, thereby generating a normalized cDNA library. The procedure has several advantages. First of all, because an excess of **complementary nucleic acid** mols. (**antisense** RNA) is used, there is no competition between full-length and truncated versions for complementary fragments and therefore there is no bias against longer clones. Second, since the synthesis is driven by an RNA promoter, even those clones without tail will be represented in the normalized library. Third, since the driver concn. is high, a Cot of 5-50 can be achieved in a few hours of incubation, thus making the procedure much quicker. Finally, only one step of hydroxylapatite purifn. is required, thus making the procedure considerably simpler and quicker. The procedure was applied to cDNA libraries from human placenta, breast tissue, pineal gland, retina, and ovarian tumor.

L31 ANSWER 21 OF 28 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 124:309560 CA

TITLE: Target nucleic acid sequence amplification and detection using linear single-strand vector probe whose **circular** form transforms bacteria and method's forensic and clinical applications



INVENTOR(S): Marcolini, Stanislavo; Martinazzo, Giorgio  
 PATENT ASSIGNEE(S): Raggio-Italgene S.P.A., Italy  
 SOURCE: PCT Int. Appl., 29 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE         |
|---|------|----------|-----------------|--------------|
| WO 9603525  | A1   | 19960208 | WO 1995-EP2944  | 19950725 <-- |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT |      |          |                 |              |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  |      |          |                 |              |
| AU 9533424  | A1   | 19960222 | AU 1995-33424   | 19950725 <-- |
| PRIORITY APPLN. INFO.:  |      |          | GB 1994-14934   | 19940725     |
|   |      |          | WO 1995-EP2944  | 19950725     |

AB A method for the detection of a target nucleic acid sequence in a sample, which comprises: (i) contacting the sample, which has been treated to bring any **nucleic acids** present into **single-stranded** form, (a) with a linear stranded vector-probe capable of transforming competent bacteria when in **circular** form, said vector-probe comprising a **nucleic acid** sequence **complementary** to the target nucleic acid sequence, and nucleic acid sequence being present in two parts, one part of said nucleic acid being present at the 5'-end of the vector-probe, the other part being present at the 3'-end, said vector-probe also comprising a region encoding a selectable or detectable marker, under conditions that permit hybridization of any target sequence present in the sample to the complementary sequence, and (b) with an enzyme capable of repairing a single-stranded break in a double-stranded nucleic acid structure; (ii) inactivating the repair enzyme; (iii) sepg. any resulting **circularized** single stranded linear vector-probe from the annealed target; (i.v.) contacting the **circularized** single stranded linear vector-probe, optionally in the form of the reaction mixt. resulting from step (ii), with competent host bacteria that lack the marker present in the vector-probe under transformation conditions; (v) culturing the resulting transformed bacteria and investigating the presence of the marker; and a vector for use in the method. The method may also be used for the detection and/or identification of mutations in a target nucleic acid sequence.

L31 ANSWER 22 OF 28 CA COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 122:126440 CA  
 TITLE: Solvent, pH, and ionic effects on the binding of **single-stranded DNA** by **circular** oligodeoxynucleotides  
 AUTHOR(S): D'Souza, David J.; Kool, Eric T.  
 CORPORATE SOURCE: Dep. Chem., Univ. Rochester, Rochester, NY, 14627, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(8), 965-70  
 CODEN: BMCLE8; ISSN: 0960-894X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effects of changing soln. conditions on the strength of triple helical complexes formed between pyrimidine-rich **circular** DNA oligonucleotides and their homopurine complements are examd. The

complexes display properties different from those seen for other types of DNA triplexes.

L31 ANSWER 23 OF 28 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 120:238465 CA  
TITLE: Molecular recognition by **circular** oligonucleotides. Strong binding of **single-stranded DNA** and **RNA**.  
[Erratum to document cited in CAl16(1):2426f]  
AUTHOR(S): Prakash, Gautam; Kook, Eric T.  
CORPORATE SOURCE: Dep. Chem., Univ. Rochester, Rochester, NY, 14627, USA  
SOURCE: Journal of the Chemical Society, Chemical Communications (1994), (5), 676  
CODEN: JCCCAT; ISSN: 0022-4936  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The errors were not reflected in the abstr. or the index entries.

L31 ANSWER 24 OF 28 CA COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 116:2426 CA  
TITLE: Molecular recognition by **circular** oligonucleotides. Strong binding of **single-stranded DNA** and **RNA**  
AUTHOR(S): Prakash, Gautam; Kool, Eric T.  
CORPORATE SOURCE: Dep. Chem., Univ. Rochester, Rochester, NY, 14627, USA  
SOURCE: Journal of the Chemical Society, Chemical Communications (1991), (17), 1161-3  
CODEN: JCCCAT; ISSN: 0022-4936  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Pyrimidine-rich **circular** DNA oligonucleotides display very high binding affinities for complementary RNA and DNA oligomers by forming bimol. triple-helical complexes.

L31 ANSWER 25 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
ACCESSION NUMBER: 2000:27036 SCISEARCH  
THE GENUINE ARTICLE: 269WH  
TITLE: **Circular antisense** oligonucleotides inhibit growth of chronic myeloid leukemia cells  
AUTHOR: Rowley P T (Reprint); Kosciolk B A; Kool E T  
CORPORATE SOURCE: UNIV ROCHESTER, DIV GENET, BOX 641, ROCHESTER, NY 14642 (Reprint); UNIV ROCHESTER, DEPT MED, ROCHESTER, NY 14642; UNIV ROCHESTER, DEPT CHEM, ROCHESTER, NY 14642  
COUNTRY OF AUTHOR: USA  
SOURCE: MOLECULAR MEDICINE, (OCT 1999) Vol. 5, No. 10, pp. 693-700.  
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010.  
ISSN: 1076-1551.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE; CLIN  
LANGUAGE: English  
REFERENCE COUNT: 32

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Background: **Antisense** represents a conceptually powerful method for regulating gene expression. However, **antisense** oligonucleotides developed to date manifest two serious limitations-nuclease susceptibility and nonspecific hybridization. **Circular** oligonucleotides may be superior to conventional linear oligonucleotides in both respects. First, **circular** agents, having no ends, are exonuclease-resistant. Second, they bind to complementary strands of RNA and DNA with a higher affinity than

corresponding linear agents.

Methods and Results: We assessed the activity of **circular** phosphodiester deoxynucleotides using chronic myeloid cell lines by targeting polypurine sequences. To represent cells having a bcr3/abl2-type junction, we used K562 cells. A **circle** targeting a bcr polypurine sequence 385 nucleotides 5' to the junction decreased the cell number by day 5 with an IC50 of 9  $\mu$ M. To represent cells having a bcr2/abl2-type junction, we used BV173 cells. A **circle** targeting the bcr-abl junction itself decreased the cell number by day 7 with an IC50 of 8  $\mu$ M. Control oligonucleotides, whether the same sequence uncircularized or **circles** with the same nucleotide composition but in scrambled sequence, had little effect. Unlike linear agents, **circles** were stable when incubated in 10% serum. The amount of ba-abl protein detected by Western blotting using a specific anti-ba-abl antibody at 24 hr in **antisense**-treated BV173 cells was only 10% of that of cells treated with control **circles**, which demonstrates an **antisense** mechanism of action.

Conclusions: **Circular** oligodeoxyribonucleotides (1) inhibit the accumulation of CML cells, (2) decrease the amount of bcr-abl protein per cell, (3) have sequence-selective activity, and (4) are more active than linear oligonucleotides containing only the base-pairing region.

L31 ANSWER 26 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 1998:466314 SCISEARCH

THE GENUINE ARTICLE: ZT689

TITLE: Replication and control of **circular** bacterial plasmids

AUTHOR: delSolar G; Giraldo R; RuizEchevarria M J; Espinosa M; DiazOrejas R (Reprint)

CORPORATE SOURCE: CSIC, CTR INVEST BIOL, VELAZQUEZ 144, E-28006 MADRID, SPAIN (Reprint); CSIC, CTR INVEST BIOL, E-28006 MADRID, SPAIN

COUNTRY OF AUTHOR: SPAIN

SOURCE: MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS, (JUN 1998) Vol. 62, No. 2, pp. 434-&. Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171. ISSN: 1092-2172.

DOCUMENT TYPE: General Review; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 350

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB An essential feature of bacterial plasmids is their ability to replicate as autonomous genetic elements in a controlled way within the host. Therefore, they can be used to explore the mechanisms involved in DNA replication and to analyze the different strategies that couple DNA replication to other critical events in the cell cycle. In this review, we focus on replication and its control in **circular** plasmids. Plasmid replication can be conveniently divided into three stages: initiation, elongation, and termination. The inability of DNA polymerases to initiate de novo replication makes necessary the independent generation of a primer. This is solved in **circular** plasmids, by two main strategies: (i) opening of the strands followed by RNA priming (theta and strand displacement replication) or (ii) cleavage of one of the DNA strands to generate a 3'-OH end (rolling-**circle** replication). Initiation is catalyzed most frequently by one or a few plasmid-encoded initiation proteins that recognize plasmid-specific DNA sequences and determine the point from which replication starts (the origin of replication). In some cases, these proteins also participate directly in the generation of the primer. These initiators can also play the role of pilot proteins that guide the assembly of the host replisome at the

plasmid origin. Elongation of plasmid replication is carried out basically by DNA polymerase III holoenzyme (and, in some cases, by DNA polymerase I at an early stage), with the participation of other host proteins that form the replisome. Termination of replication has specific requirements and implications for reinitiation, studies of which have started. The initiation stage plays an additional role: it is the stage at which mechanisms controlling replication operate. The objective of this control is to maintain a fixed concentration of plasmid molecules in a growing bacterial population (duplication of the plasmid pool paced with duplication of the bacterial population). The molecules involved directly in this control can be (i) RNA (**antisense** RNA), (ii) DNA sequences (iterons), or (iii) **antisense** RNA and proteins acting in concert. The control elements maintain an average frequency of one plasmid replication per plasmid copy per cell cycle and can "sense" and correct deviations from this average. Most of the current knowledge on plasmid replication and its control is based on the results of analyses performed with pure cultures under steady-state growth conditions. This knowledge sets important parameters needed to understand the maintenance of these genetic elements in mixed populations and under environmental conditions.

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 ACCESSION NUMBER: 95:406575 SCISEARCH  
 THE GENUINE ARTICLE: RB956  
 TITLE: SYNTHESIS OF **CIRCULAR** OLIGODEOXYNUCLEOTIDE  
 CONJUGATES VIA TRANSIENT ABASIC SITES  
 AUTHOR: PEOCH D; IMBACH J L; RAYNER B (Reprint)  
 CORPORATE SOURCE: UNIV MONTPELLIER 2, CHIM BIOORGAN LAB, CNRS, URA 488, CASE  
 008, PL EUGENE BATAILLON, F-34095 MONTPELLIER, FRANCE  
 (Reprint); UNIV MONTPELLIER 2, CHIM BIOORGAN LAB, CNRS,  
 URA 488, F-34095 MONTPELLIER, FRANCE  
 COUNTRY OF AUTHOR: FRANCE  
 SOURCE: NUCLEOSIDES AND NUCLEOTIDES, (1995) Vol. 14, No.  
 3-5, pp. 847-850.  
 ISSN: 0732-8311.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: ENGLISH  
 REFERENCE COUNT: 7

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB New chemical ligation or cyclisation reactions, using high reactivity  
 of abasic sites with amines, are reported for the synthesis of  
 oligonucleotide clamps and single-stranded **circular**  
 oligonucleotides. Thermal denaturation experiments show that these  
 molecules display very high binding affinities for **complementary**  
 DNA **oligomer** by forming triple-helical complexes.

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 ACCESSION NUMBER: 95:131940 SCISEARCH  
 THE GENUINE ARTICLE: QG046  
 TITLE: HISTONES ASSOCIATED WITH **SINGLE-STRANDED**  
**-DNA** DO NOT PRECLUDE THE FORMATION OF  
 DOUBLE-HELICAL DNA  
 AUTHOR: FERNANDEZBUSQUETS X; DABAN J R (Reprint)  
 CORPORATE SOURCE: UNIV AUTONOMA BARCELONA, FAC CIENCIES, DEPT BIOQUIM & BIOL  
 MOLEC, E-08193 BARCELONA, SPAIN (Reprint); UNIV AUTONOMA  
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 E-08193 BARCELONA, SPAIN  
 COUNTRY OF AUTHOR: SPAIN  
 SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-GENE STRUCTURE AND  
 EXPRESSION, (25 JAN 1995) Vol. 1260, No. 2, pp.  
 132-138.

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AB The effect of histones on the reaction of reassociation of the two complementary strands of DNA from different sources has been investigated. The reassociation rate of denatured linear DNA from bacteriophage M13 monitored spectrophotometrically and using nuclease S1 is roughly the same in the presence and absence of core histones at physiological ionic strength. Electron microscopy reveals that in the samples containing histones a large network of duplex DNA is produced. Nevertheless, closed **circular** M13 DNA and a cloned DNA fragment (158 bp) from nucleosomal origin are entirely renatured in the presence of histones as demonstrated by the well-defined double-stranded DNA bands seen in electrophoretic gels. Various experiments performed using the purified (+) and (-) strands of the cloned nucleosome DNA fragment at low ionic strength indicate that core histones initially bound to one or even to the two strands allow the formation of duplex DNA. These findings and the results obtained with partially denatured closed **circular** M13 DNA allow us to conclude that core histones neither prevent the nucleation nor inhibit the rapid zippering reactions leading to the formation of double-stranded DNA. The mechanism that allows the renaturation of DNA in the presence of histones may also participate in biological processes involving the pairing of **complementary nucleotides**.